Original Article

Anemia and Thrombocytopenia in Malaria: An Observational Study of 115 Patients in Mardan, Pakistan.

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Objective: The aim of present study was to evaluate hematological changes in malaria in Mardan, Pakistan.

Methods: This prospective observational study was conducted at O.P.D of Mardan Medical Complex Mardan from July to September 2015. A total of 115 patients were divided to age groups of <15 and > 15 years old. Malaria parasite was examined using thick and thin smears stained with Giemsa stain and also cross-checked by ICT. Those patients with a confirmed diagnosis of malaria were investigated for platelets, hemoglobin and total leukocyte count on Automatic hematology analyzer (Mindray) and studied by hematologist. Data was tabulated, descriptive statistics analyzed; the chi-square test was applied to evaluate statistical significance of the studied variable between groups on SPSS version 20. A p-value of 0.05 or less was used for statistical significance.

Results: A total of 115 patients were included in the study. Male were 56(48.7%) and females 59(51.3%), the mean age of study group was 10.62(3.89). According to age group, patients were divided into two groups; those <15 years comprised of 102(88.7%), while > 15 years were found 13(11.3%). P. vivax was seen in 108(93.9%) and P. falciparum 7(6.1%) patients. Out of total population 70(60.9%) were found anemic, 79(68.7%) had mild thrombocytopenia and 4(3.5%) with moderate thrombocytopenia and sever leucopenia were found 2(1.7%), mild leucopenia 24(20.9%), mid leucocytosis 1(0.9%). Patients with P.vivax aged <15 years had found anemia 59(62.1%) with p=0.56, moderate thrombocytopenia 4(4.2%) (p=0.05), sever leucopenia 2(2.11%), mild leucopenia 13(13.7%) and mild leukocytosis 1(1.1%) with p=0.001.

Conclusions: The present study concludes that thrombocytopenia and anemia are common hematological findings in patient with Plasmodium infection particularly vivax species infection in Mardan region. Therefore, malaria should be a consideration in febrile patients with low platelets and haemoglobin.

Keywords: Malaria, anemia, leucocyte, thrombocytopenia.

Introduction

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.[1] Four species of Plasmodium can cause malaria in human beings. These include Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale and Plasmodium malariae.[2]

According to World Health Organization assessment, about 40% of the world population is at risk of developing malaria. About 300-500 million people are infected with it.[3] Every year about 2 million people die due to malaria and its complications.[4] The highest mortality is in Africa, mainly in young children. 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 %.[5] Malaria is associated with high mortality and morbidity all over the world. Malaria results in the loss of 35,728000, Disability Adjusted Life Years revealing the worldwide impact of this disease.[6] Geographical distribution of the disease is worldwide, being found in tropical areas, throughout Sub-Saharan Africa and to a lesser extent in Southeast Asia, South Africa, the Pacific Islands, India and Central and South America. Pakistan is among the countries having a high infectivity rate of malaria. The Directorate of Malaria Control has reported that one person per thousand in the population is infected with malaria.[7] Active malarial transmission happens throughout the year, while aggressive out bursts of disease are seen mainly during and after the 'monsoon' season.

Malaria is usually associated with various degrees of reduced blood counts. Though the anemia is hemolytic in nature, the hemopoietic response is blunted, as evidenced by disproportionate reticulocytes counts, reduced platelets and WBC

counts indicating some blem with manufacturing apparatus. Mild or moderate thrombocytopenia is a common association of malaria and is rarely associated with hemorrhagic manifestations or a component of disseminated intravascular coagulation.[8,9,10] Thrombocytopenia has been reported in the majority of malaria studies[11,12,13,14,15] Laboratory alterations associated with malaria are well recognized but specific changes may vary with level and type malaria endemicity, demographic factors and malaria immunity.[16] The aim of the present study was to determine evaluate hematological changes in malaria in Mardan, Pakistan.

Methods

This prospective observational study was conducted at O.P.D of Mardan Medical Complex with the facilities of clinical laboratory. The duration of study was from July to August 2015. Patients with fever and positive MP slide were included in the study and all patients with fever but negative for MP slide were excluded from the study. Both the thick and thin films were advised to the patients. A total of 115 patients were divided to age groups of <15 and > 15 years old. Malaria parasite was examined using thick and thin smears stained with Giemsa stain and also cross-checked by ICT. Those patients with a confirmed diagnosis of malaria were investigated for platelets, hemoglobin and total leukocyte count on Automatic hematology analyzer (Mindray) and studied by hematologists. On the basis of hemoglobin, two groups were classified as group A having hemoglobin < 10 gm/dL and group B having hemoglobin >10 gm/dL. The normal range of leukocytes was taken as 400011000/cmm, any deviation from this limit was noted as abnormal.
Thrombocytopenia was defined as mild (Plat 50-150x103cells/ul), moderate (Plat 20-50x103cells/ul) and severe (Platelets <20x103cell/ul).17 All the data were tabulated, descriptive statistics were analyzed, and the chi-square test was applied to evaluate statistical significance of the studied variable between groups on SPSS version 20, A p-value of 0.05 or less was used for statistical significance.

Results

A total of 115 patients were included in the study. Male were 56(48.7%) and females 59(51.3%), the mean age of study group was 10.62(3.89). According to age group, patients were divided into two groups; those <15 years comprised of 102(88.7%), while > 15 years were found 13(11.3%). **Table 1,** P. vivax was seen in 108(93.9%) and P. falciparum 7(6.1%) patients. **Figure 1.**
According to laboratory findings; out of total population 70(60.9%) were found anemic, 79(68.7%) had mild thrombocytopenia and 4(3.5%) with moderate thrombocytopenia and sever leucopenia were found 2(1.7%), mild leucopenia 24(20.9%), mid leucocytosis 1(0.9%). **Table 2 &Figure 2.**
According to the type of malaria and age group; patients with P.vivax aged <15 years had found anemia 59(62.1%) with p=0.56, moderate thrombocytopenia 4(4.2%) (p=0.05), sever leucopenia 2(2.11%), mild leucopenia 13(13.7%) and mild leukocytosis 1(1.1%) with p=0.001. Patients with P. vivax and age > 15 years had found; anemia 7(53.8%), mild thrombocytopenia 6(46.2%) and mild leucopenia 8(61.5%).**Table 3**
Patients with P. falciparum malaria aged < 15 years had found; anemia 4(57.1%) with p=0.48, mild thrombocytopenia 4(57.1%) and mild leucopenia 1(25%) and patients with age> 15 years had found; anemia 4(57.1%), mild thrombocytopenia 4(57.1%) and mild leucopenia 3(42.9%) with p=0.37. **Table 3**

Table-1: Age and sex distribution n=15.

Sex	Frequency	Percentage
Male	56	48.7
Female	59	51.3
Age<15 years	102	88.7
Age> 15 years	13	11.3
Total	115	100

Table-2: Laboratory profile n=115.

Variable		Frequency	Percentage
Hb	Anemia	70	60.9
	No anemia	45	39.1
Platelets	Normal	32	27.8
	Mild thrombocytopenia	79	68.7
TLC	Moderate thrombocytopenia	4	3.5
	Severe peucopenia	2	1.7
	Mild leucopenia	24	20.9
	Mild leucocytosis	1	0.9

Table-3: Profile of P.vivax, P. Falciparum according to age group.

Malaria		Age Group <15 years n=102	>15 years n=13	Total	P-value
P. Vivax	Anemia	59 (62.1%)	7 (53.8%)	66 (61.1%)	0.56
N=108 Hb	No Anemia	36 (85.7%)	6 (14.3%)	42 (38.9%)	
	Moderate Thrombocytopenia	4 (4.2%)	0 (0.0%)	4 (3.7%)	0.05
Platelets	Mild Thrombocytopenia	69 (72.6%)	6 (46.2%)	75 (69.4%)	
	Normal platelets	22 (23.2%)	7 (53.2%)	29 (26.9%)	
	Severe leucopenia	2 (2.11%)	0 (0.0%)	2 (1.9%)	
TLC	Mild leucopenia	13 (13.5%)	8 (61.5%)	21 (19.4%)	
	Normal	19 (94.0%)	5 (38.5%)	84 (77.8%)	
	Mild leukocytosis	1 (1.1%)	0 (0.0%)	1 (0.9%)	0.001
	Moderate leukocytosis	Nil	Nil	Nil	
	Severe leukocytosis	Nil	Nil	Nil	
P. Vivax	Anemia	4 (57.1%)	Nil	4 (57.1%)	0.48
N=7 Hb	No Anemia	3 (25%)	Nil	3 (42.9%)	
Platelets	Moderate Thrombocytopenia	Nil	Nil	Nil	
	Mild Thrombocytopenia	4 (57.1%)	Nil	4 (57.1%)	
TLC	Normal platelets	4 (42.9%)	Nil	3 (42.9%)	0.37
	Severe leucopenia	Nil	Nil	Nil	
	Mild leucopenia	1 (25%)	2 (66.7%)	3 (42.9%)	
	Normal	3 (75%)	1 (33.3%)	4 (57.1%)	
	Mild leukocytosis	Nil	Nil	Nil	
	Moderate leukocytosis	Nil	Nil	Nil	
	Severe leukocytosis	Nil	Nil	Nil	

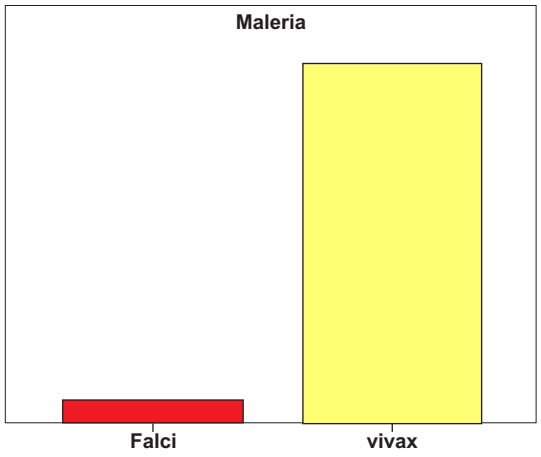

Fig-1: Frequency of marlaria type n=115.

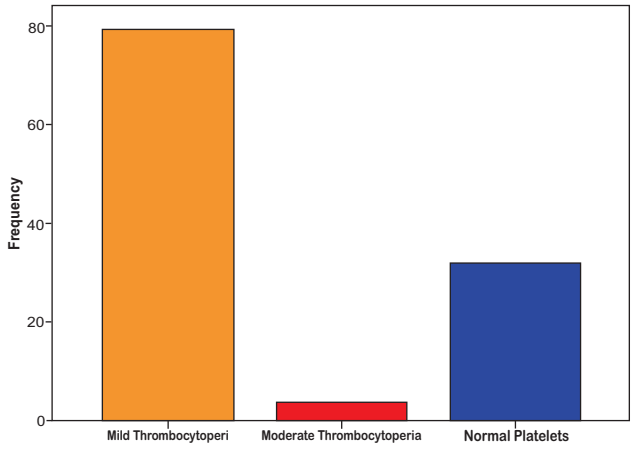

Fig-2: Frequency of thrombocytopenia n=115.

Discussion

The hematological changes related with malaria are familiar, but precise changes may vary with category of malaria, with the background of hemoglobinopathy, nutritional status, demographic factors and malaria immunity. [18] In this study, the frequency of P. vivax was higher 108 (93.9%) as compared to P. falciparum 7(6.1%). A study conducted by Bega et al, in a tertiary care hospital in Karachi which showed P. vivax in 52% and P. falciparum in 46% of patients with acute malaria.[19] In other study, P. vivax was detected in 54% and P. falciparum in 39% in the pediatric age group studied by Jalaluddin which showed a higher frequency of P. falciparum as compared to P. vivax (65% vs. 35%) in children.[20]

Present study reported thrombocytopenia out of the total population was 79(68.7%) as mild and 4(3.5%) as moderate thrombocytopenia. In cases of P.vivax and age > 15 years reported moderate thrombocytopenia 6(46.2%) and in P. falciparum it was 4(57.1%). A study conducted by Qurban et al, reported 93.33% of thrombocytopenia in patients having Plasmodium vivax.[21] In contrast to our study Jadhav and Patkar conducted an extensive study regarding pattern of thrombocytopenia in patients having vivax and falciparum malaria. They documented thrombocytopenia in both groups of patients but severe thrombocytopenia, (platelets 20,000 or less) was more consistent with Plasmodium falciparum malaria, [22] while Memon has reported thrombocytopenia in malaria to be about 70%.[23] Platelets may play a role in the pathophysiology of severe malaria. Malaria is associated with a pro-coagulant tonus characterized by thrombocytopenia, activation of coagulation cascade and fibrinolytic system. However, bleeding and hemorrhage are uncommon; suggesting that a compensated state of blood coagulation activation occurs in malaria.[24] The degree of thrombo- cytopenia has been considered a criterion of disease severity by David, et al. in the United Kingdom.[25] Thrombocytopenia may result from a shortened life span of the platelets or from pooling and destruction in the spleen.[26]

Present study reported 79(68.7%) anemia out of total studied population, of which 59(62.1%) anemic cases were < 15 years old and 7(53.8%) under 15 years age group. Anemia was also reported in 56.45% of malaria patients by Qurban et al, as another hematological indicator.[21] The etiology of anemia in malaria is multi-factorial. It may be due to intravascular haemolysis, splenic removal of the infected cells, immune complex adsorption onto erythrocyte membranes, effects of therapeutic agents on parasitized cells and bone marrow erythroid hypoplasis.[27] Furthermore, some observers have suggested that malaria-related anemia is more severe in the areas of intense malaria transmission and in younger children rather than older children or adults.[28] The hemoglobin changes observed in this study population may reflect a higher prevalence of underlying anemia, poor nutritional status and non-availability of proper treatment.

Present study found sever leucopenia 2(1.7%), mild leucopenia 24(20.9%) and mild leucocytosis 1(0.9%) of the total studied population. According type of malaria and age group, P. vivax infected patients with age less than 15 years found sever leucopenia 2(2.11%), mild leucopenia 13(13.7%) and mild leucocytosis 1(1.1%), and in patients > 15 years old had mild leucopenia 8(61.5%). Patients of P.falciparum with age < 15 years had mild leucopenia 1(25%) and with age > 15 years had mild leucopenia 3(42.9%).

A study of malaria and hematological changes reported mild to moderate leucopenia characterized by decreased neutrophils, left shift and moncytosis .[29] Leucopenia is thought to be due to the localization of leucocytes away from peripheral circulation, splenic sequestration and other marginal pools rather than actual depletion or stasis.[30] Leucocytosis may suggest co-existing viral infection particularly in the presence of atypical lymphocytes common in children with concurrent viral infections.[31] Many recent studies also show leucocytosis among the malaria patients. Adedapo et al, reported leucocytosis in about 9.5% of the patients with malaria.[31] Leukocytosis may also have some relation with poor prognosis of disease, in relation to the value of leucocytosis in malaria. Studies have been conducted in P. falciparum infected African children with similar results showing poor prognosis.[32] A co-existing viral infection should always be considered in patients presenting with acute malaria and leucocytosis. In case of neutrophilic leukocytosis, intravascular hemolysis, disseminated intravascular coagulation or additional bacterial infection must be investigated.

Conclusion

Thrombocytopenia and anemia were common hematological findings in patient with Plasmodium infection particularly marked in vivax species

infection. Therefore, malaria should be a consideration in febrile patients with low platelets and haemoglobin. Patients with acute febrile illness having combination of thrombocytopenia and anaemia should alert the treating physician about the possibility of malaria infection which can be confirmed with specific tests.

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Answer Picture Quiz

Large pneumoperitoneum following PEG placement attempt

During the procedure the wire had difficulty advancing externally from the stomach and was noted to be tense. General surgery was consulted and the area of the incision was extended. The wire was then extracted, and during the extraction there was an audible "pop." Post procedure the patient had abdominal distention and increased work of breathing as well as dyspnea and hypoxia. He required 100% non-rebreather oxcygen and was saturating below 90% for approximately one hour. His chest and upper abdominal x-ray was significant for pneumoperitoneum. However, his abdominal distention and respiratory status would improve over the next several hours and a repeat x-ray performed less than 6 hours later showed complete resolution of subdiaphragmatic air. The patient had PEG placement performed 2 days later without complication. Pneumoperitoneum following percutaneous endoscopic gastrostomy tube placement is a common complication. Its incidence is noted to be approximately 20% in one series. Amongst these cases, only 4.6% had subdiaphragmatic air visualized after 72 hours and none of these cases were found to be clinically significant. CO2 has been increasingly used for insufflation due to its rapid absorption and has been shown to reduce the frequency of post-PEG pneumoperitoneum .