Investigation of Thrombocytopenia in Patients of Malaria

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Abstract

Protozoan parasites of the genus *Plasmodium* cause malaria, a devastating disease prevalent across tropical regions around the world. In the year 2016, more than 216 million clinical cases and 445,000 deaths were reported across 91 countries worldwide This scientific research has started and ended in the period of 2 years, conducted from 2/1/2018 to 5/8/2019 in the infectious wards/branches of the Nangarhar medical faculty's. **Materials and Methods:** We conducted this study to find out the frequency and the degree of thrombocytopenia in patients with malaria. In our study, 180 patients with malaria positive were investigated with platelet count. **Results:** In the study group of 180 patients: 101 (56.11%) were positive for Plasmodium vivax, 70 (38.88%) were positive for P. falciparum and 9 (5.00%) had mixed infection with both P. vivax and P. falciparum. Out of 101 cases detected with vivax malaria, 77 cases had thrombocytopenia. Out of 70 cases detected with falciparum malaria, 54 cases had thrombocytopenia. Among 9 cases of mixed infection, 6 cases had thrombocytopenia. **Conclusions**: Presence of thrombocytopenia in a patient with acute febrile illness in the tropics increases the possibility of malaria. The above finding can have therapeutic implications in context of avoiding unnecessary platelet infusion in malaria patients.

KEY WORDS: Malaria, Plasmodium falciparum, Plasmodium vivax, thrombocytopenia

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Introduction

Protozoan parasites of the genus *Plasmodium* cause malaria, a devastating disease prevalent across tropical regions around the world. In the year 2016, more than 216 million clinical cases and 445,000 deaths were reported across 91 countries worldwide [16]. Nearly half of the world's population is at risk of malaria infections. In Southeast Asia alone, >1.4 million clinical cases and >550 deaths occur every year due to malaria. In India, during 2016, ~1.09 million clinical cases and 331 deaths were reported [17]. At present, about 109 countries in the world are considered endemic for malaria. 45 countries within the WHO African regions. An estimated 3.3 billon people were at risk of malaria in 2006. Of this Total, 2,1 billons were at low risk (<1 reported case per 1000 population), 97 per cent of home were living in regions other than Africa. the 1,2 billon were at high risk (≤ 1 case per 1000 population) were living mostly in the WHO African (49 %) and South Asia regions (37%) [12]. Mangaluru is the administrative headquarters of Dakshina Kannada district of Karnataka state in southern India. This coastal city is surrounded by Netravati and Gurupura rivers and is located between the waters of Arabian Sea and hills of Western Ghats. Since 1930, Mangaluru city has been fighting malaria and is still considered to be endemic in this region [7, 2]. In 2017, among the 11312 malarial cases reported in the Karnataka state, Mangaluru alone contributed to 8075 (71.4%) cases. Two major species of

Plasmodium, namely, *P. vivax*, Pv, (6452, 79.9%) and *P. falciparum*, Pf, (1623, 20.1%) infections are prevalent in the city and its surrounding regions. The malarial infections are common throughout the year in this region with its peak transmission during the rainy season, between the months of June to September [3]. *Plasmodium vivax* is the most geographically widespread species of human malaria parasites, affecting almost 40% of the world's population [12–6]. The invisibility of the dormant liver stages of *P. vivax* to any diagnostic method may lead to an underestimation of the true prevalence of *P. vivax* far more than *P. falciparum*. This means *P. vivax* parasites could be highly prevalent in many endemic settings [6]. Most recorded *P. vivax* malaria cases originate from South East Asia and the Western Pacific, and a significant number also occur in Africa and South America [12–9]. Immunopathological studies have shown that platelets are an important component of the host innate immune responses against malaria infection [10]. Thrombocytopenia (platelet count $< 150\,000/mm^3$) appears to be a very frequent hematological alteration in acute malaria infections [18, 11–15]. Severe malaria is defined by a demonstration of asexual forms of the malaria parasites in the blood of a patient with a potentially fatal manifestation or complication of malaria in whom other diagnoses have been excluded [9, 18]. In brief, the clinical features of severe falciparum malaria are impaired consciousness, prostration, multiple convulsions, acute respiratory distress, circulatory collapse or shock, acute kidney injury, clinical jaundice and abnormal bleeding [19]. Although thrombocytopenia is not included in the current World Health Organization (WHO) criteria for defining severe *P. falciparum* malaria [17]. Malaria is a Protozoal disease caused by infection with parasites of the genus Plasmodium and transmitted to man by certain species of infected female Anopheline mosquito. Five species of Plasmodium (Plasmodium vivax, Plasmodium falciparum, Plasmodium malaria, Plasmodium oval, and Plasmodium Knowles) cause malaria in humans. In 2008, there were an estimated 243 million cases of malaria world-wide. A vast majority, about 85% were in African Region, followed by the South-East Asia Region (10%) and East Mediterranean (4%). Malaria accounts for an estimated 863,000 deaths, of which 89% were in African Region followed by East Mediterranean (6%) and South-East Asia Region (5%) [1]. In India about 27% population lives in malaria high transmission area (more than 1 case per 1000 population) and 58% in low transmission area.[2] In 2008 there were 1.52 million cases of malaria in India, out of which 0.76 million case of P. falciparum, comprising 50% of total malaria cases. There were 924 deaths from malaria [1]. A typical attack of malaria comprises three distinct stages: Cold stage, hot stage and sweating stage. The clinical features of malaria vary from mild to severe, and complicated, according to the species of parasite present, the patient's state of immunity, the intensity of infection and also the presence of concomitant conditions such as malnutrition and other diseases. Malaria parasite affects multiple organs of the body such as liver, spleen, brain, gastro intestinal tract, gall bladder, pancreas, blood vessels and placenta. Hence the clinical picture could be of wide spectrum ranging from simple malaise to life threatening central nervous symptoms like coma. Hematological abnormalities have been observed in patients with malaria, with anemia, and thrombocytopenia being the most common [16,8]. A number of observational studies have confirmed the association of thrombocytopenia to malaria. Both non-immunological as well as immunological destruction of platelets have been implicated in causing thrombocytopenia. The speculated mechanisms are coagulation disturbances, sequestration in spleen, antibody mediated platelet destruction, oxidative stress,

and the role of platelets as cofactors in triggering severe malaria. Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malaria parasites [4]. We conducted this study to find out the frequency and the degree of thrombocytopenia in patients with malaria. Platelet counts of 75,000 to 150,000/µl are defined as grade 1 thrombocytopenia, 50,000 to <75,000/ µl as grade 2, 25,000 to <50,000/ µl as grade 3, and below 25,000/ µl as grade 4 thrombocytopenia. (CTCAE v3.0; www.ctep.cancer.gov/reporting/ctc.html),here we use this criteria for the classification of thrombocytopenia in vivax malaria patients.

MATERIALS AND METHODS

The blood investigations were carried out in the central lobotry of infectious wards/branches of the Nangarhar medical faculty's to those patients who were referred to pathology laboratory for malaria test from various departments especially, from internal medicine and pediatrics. Written consent had been taken from the patients. This prospective study was carried out from 2/1/2018 to 5/8/2019. A total 180 patients were included for studies that were found the positive for malaria parasite. Malaria test was carried out by thin and thick smear examination. Thin smear was stained by Leishman stain and thick smear was stained by field stain. In field stain polychromated methylene blue and eosin stains specifically to basophilic and acidophilic cellular elements to demonstrate blood cells and hemoparasites. All patients undergone for complete blood count by a fully automated hematology. Data were analyzed by SPSS-20 method. They reported thrombocytopenia in 61.5% children and bleeding symptoms in 10.8% cases. A study from Venezuela reported thrombocytopenia in 58.9% children with P. vivax malaria, with 25.6% requiring platelet transfusions.

RESULTS

In our study, 180 patients with malaria positive were investigated with platelet count. Out of 180 patients 113 (62.77%) were males and 67 (37.22%) were female. Age of patients was between 2 year and 65 years with a majority of the patients between 17 years and 43 years of age. A total 48 (26.66%) patients were belonging to pediatric age group.

Table 1. Age and sex distribution of study groups

1	Ages %	Male %	Female %	Total %
2	2 – 18	30 (26.54 %)	19(28.35%)	49(54.80%)
3	19 – 30	37 (32.74 %)	23(34.32%)	60(67.06%)
4	31 – 45	23 (20.35 %)	18(26.86%)	41(47.21%)
5	46 – 65	23 (20.35 %)	7 (10.44%)	30(30.79%)
6	Total	113 (99.98 %)	67(99.97%)	180(199.86%)

Mean hemoglobin value was 13.0 g% and mean white blood cell count was 12,000 /cumm , Mean platelet count was 151,000/cumm All the patients had fever (100%) at the time of presentation, followed by weakness (94%), nausea (90%), vomiting (85%), anorexia (81%) and diarrhea (1.1%). Most common sign was anemia (80%) followed by splenomegaly (26.11%),

jaundice (13.33%), and hepatomegaly (2.77%). One patient was having cerebral malaria. The spontaneous bleeding and mortality was not seen.

Table 2 : Frequency of clinical features in patients with malaria

Symptoms/sign	Clinical feature	No of patients	%
Symptoms	Fever	180	100%
	Weakness	172	94%
	Nausea	162	90%
	Vomiting	155	85%
	Anorexia	144	81%
	Diarrhea	2	1.11%
Signs	Anemia	144	80%
	Splenomegaly	36	26.11%
	Jaundice	18	13.33%
	Hepatomegaly	3	2.77

In the study group of 180 patients: 101 (56.11%) were positive for P. vivax, 70 (38.88%) were positive for P. falciparum and 9 (5.00%) had mixed infection with both P. vivax and falciparum. Out of 101 cases detected with vivax malaria, 77 cases had thrombocytopenia, 23 (29.87%) cases had normal platelet count. 15 (19.48%) cases had Grade I thrombocytopenia. 19 (%) cases had Grade II thrombocytopenia, 30 (17.39%) cases had Grade III thrombocytopenia and 6 (6.51%) cases had Grade IV thrombocytopenia. Out of 90 cases detected with falciparum malaria, 70 cases had thrombocytopenia, 20 (8.69%) cases had normal platelet count, 15 (6.51%) cases had Grade I thrombocytopenia, 20 (8.69%) cases had Grade II thrombocytopenia, 35 (15.17%) cases had Grade III thrombocytopenia and no patient was detected Grade IV thrombocytopenia. Among 10 cases of mixed infection, 9 cases had thrombocytopenia, 1 (0.58%) case had normal platelet count, 3 (1.75%) cases had Grade I thrombocytopenia, 2 (1.16%) cases had Grade II thrombocytopenia, 2 (1.16%) cases had Grade III thrombocytopenia and 1 (0.58%) case had Grade IV thrombocytopenia.

DISCUSSION

Malaria caused by P. vivax and P. falciparum is endemic in many parts of Afghanistan. Malaria affects almost all blood components and is a true hematological disease. Thrombocytopenia and anemia are the most frequently malaria associated hematological complications. In endemic areas malaria has been reported as the major cause of low platelet counts. This is so characteristic of malaria, that in some places, it is used as an indicator of malaria in patients presenting with fever. Platelets count of less than 150,000/cumm increases the possibility of malaria 12-15 times. P. vivax was the common species in our study, though many of the patients who were included in our study had infection with P, vivax (56.11%) p . falciparum (38.88%) and mixed infection 9(5.00%). Faseela et al. in her study found similar results. In our study, thrombocytopenia was seen in 76.11% cases. Colonel et al., reported thrombocytopenia in 72% of patients with malaria infection. Jamal et al., in their study on pediatric patient have reported low platelet count in 72% of the patients with malaria infection. The mechanism of thrombocytopenia in malaria is not clearly Known. Thrombopoietin (TPO) is

the key growth factor for platelet production and is elevated in states of platelet depletion. TPO serum levels have been shown to be significantly higher in subjects with severe malaria, normalizing within 14-21 days of therapy. Two types of changes in platelet dysfunction are seen in malaria. Initially, there is platelet hyperactivity, this is followed by platelet hypo activity. Platelet hyperactivity results from various aggregating agents like immune complexes, surface contact of platelet membrane to malarial red cells and damage to endothelial cells. The injured platelets undergo lysis intravascularly. 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 one to two weeks. Thrombocytopenia improves with disease resolution and the platelet count is generally normal within seven days but ranged from 2-28 days in one series.

CONCLUSION

Higher frequency of mild to severe thrombocytopenia was observed in-patients suffering from malaria. The above finding can have therapeutic implications in context of avoiding unnecessary platelet infusion in malaria patients. Presence of thrombocytopenia in a patient with acute febrile illness in the tropics increases the possibility of malaria. This may be used in addition to the clinical and microscopic parameters to heighten the suspicion of this disease and prompt initiation of the treatment.

Suggestions

1) Protect yourself from mosquito bites by sleeping under an insecticide-treated mosquito net.
2) Wear socks, long pants, long-sleeve shirts and blouses.
3) Spray DEET mosquito repellent onto your clothes and the exposed parts of your skin.

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