Original Article

Thrombocytopenia in patients diagnosed with Malaria in District Buner, KP

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Abstract

Introduction: Thrombocytopenia is one of the numerous complications of malaria infection, which could be lethal if not diagnosed and managed on time. Our study aims to determine the occurrence of thrombocytopenia in patients hospitalized with malaria.

Material and Methods: A retrospective cross-sectional study was conducted between January 2016 till December 2019. Data was collected from the patient's record registers. A total of 201 cases were included in this study. Data was collected, entered, and analyzed in IBM SPSS 23 software package.

Results: Out of the total 201 cases, 108 (53.7%) were males and 93 (46.3%) were females. 189 (94%) cases were suffering from *P. vivax*, 10 (5%) were suffering from *P. falciparum,* and cases suffering from both were only 2 (1%). Thrombocytopenia was present in 183 (91.04%) cases (95% confidence interval 2.13-2.37). 91.53% (n=173) of cases diagnosed with P. vivax had thrombocytopenia while 90% (n=9) cases diagnosed with P. falciparum had thrombocytopenia.

Conclusion: We conclude from this study that, thrombocytopenia occurs in all species of malaria and is not a distinguishing feature between the principal types of malaria. With prompt identification and management, platelets count reverts back to normal.

Keywords: Malaria, Thrombocytopenia, Plasmodium vivax, Plasmodium falciparum.

Introduction

Malaria is a devastating disease caused by *Plasmodium,* a protozoan parasite.[1] Four different species of Plasmodium i-e P. falciparum, P. malariae, P. ovale, and P. vivax are the main contributors of human malaria infection. It is prevalent around the world, notably in tropical and subtropical areas.[2] Plasmodium vivax is the most geographically prevalent species out of them. Around 40% of the population of the world is affected by it.[3,4]

Malaria infection is a threat to half of the global population.[5] In 2017, 219 million clinical cases and 435,000 deaths due to malaria infection had been reported worldwide.[2] Contribution of south-east Asia is underestimated, contributing >40% burden of global infection.[5] In 2015, the estimated global mortality rate was 429,000 due to malaria. Major contributors, which is more than 36% of malaria deaths were countries in sub-Saharan Africa, with the Democratic Republic of the Congo and Nigeria together. Four countries (Ethiopia, India, Indonesia, and Pakistan) accounted for 81% of estimated deaths due to PV malaria.[6]

Pakistan has been grouped with Sudan, Yemen, Somalia, and Afghanistan under one of the highest malaria burden-sharing countries with an estimation of 1 million cases of malaria annually.[6] Regarding the high infectivity rate of malaria in Pakistan, the Directorate of Malaria Control has reported that One individual per thousand is infected with malaria.[7] There is a high variation in the prevalence of the Plasmodium parasite among different regions of Pakistan. Malaria infection is principally attributed to P. vivax, but P. falciparum but mixed infections are also prevalent.[8] Malaria is primarily found in Federally Administered Tribal Areas, followed by Baluchistan and Khyber Pakhtunkhwa.[9]

Clinically malaria has no definitive diagnostic features as it imitates many diseases clinically. It mainly affects RBCs (Red blood cells) and causing a hematological abnormality of anemia, but thrombocytopenia is also a well-known complication in almost every part of the world. It has been documented with mono-infection i-e P. falciparum and P. vivax and also with combined infection of both.[10,11]

Several observational studies have established the association of thrombocytopenia to malaria, but to this day, the cause of thrombocytopenia is not adequately understood. There is no exact mechanism known yet for malaria induced thrombocytopenia but seems to occur due to peripheral destruction, splenic sequestration, excessive consumption in the process of DIC (disseminated intravascular coagulation) immune destruction, alteration in the bone marrow and binding of platelets to infected red blood cells causing pseudo-thrombocytopenia and oxidative stress is also a contributing factor.[12] According to some recent evidence, besides the principal function of clotting, platelets are suggested to contribute to the killing of malarial parasites and clearing the infection.[13]

In various studies conducted about malaria induced thrombocytopenia, there was an incidence of 48-57% of thrombocytopenia in the malaria-affected patient.[11] In almost every case, thrombocytopenia is not linked to bleeding and requires no treatment. The platelet counts rapidly revert to normal after the successful treatment of the malarial episode, although thrombocytopenia associated with bleeding is one of the clinical manifestations of severe malaria and is one of the major causes of mortality in older infants and children(3). It has been reported that a 9-fold increase in the risk of mortality from P. vivax in children with severe anemia and severe thrombocytopenia, as compared to those without anemia or thrombocytopenia.[13] Studies have shown the association of low platelet count with an increase in mortality in patients with *P. Falciparum* and *P. vivax* infections.[15,16] A recent increase in a number of studies is seen, which have addressed the frequency of thrombocytopenia in P. vivax infection. Understanding the mechanism, occurrence, and role of thrombocytopenia in malaria may improve clinical practice guidelines and recuperate the risk of mortality in severe cases.

Materials and Methods

This research was conducted as a retrospective cross-sectional study. Data were collected from the patient's record register from January 2016 till December 2019. Data was recorded on proforma specially designed for this study. A total of 201 cases were included in this study. The research reported here was conducted in Bilal Medical Trust Hospital, a private hospital in District Buner. Buner is a district in the Malakand division of Khyber Pakhtunkhwa province in Pakistan. This hospital is a trust hospital and provides healthcare to different social classes of people all over Buner.

The inclusion criteria for this study were all the patients presenting with high-grade fever, and a diagnosis of malaria was made with thin and thick blood smear films. All patients in this endemic area

with fever are suspected to have malaria due to P. vivax, given this is the unique species in this zone.

Patients with malaria treated outside the hospital, no platelet count available before the initiation of treatment, known HIV positive status, known thrombocytopenia/platelet disorders, mean corpuscular volume (MCV) < 75 (suggesting iron deficiency anemia), known chronic renal failure or clinical diagnosis of malaria without slide positivity were excluded from the study.

Baseline platelet levels were done before initiation of treatment and then repeated on the third day for every patient after the initiation of treatment. Platelets were measured using Swelab Alfa Plus Systems. Mild thrombocytopenia was defined as platelet count 100,000 to 150,000/microL, moderate as 50,000 to 99,000/microL and severe as <50,000/microL.[17]

Ethical approval was obtained from the Ethical Review Board of Prime Foundation, Peshawar Medical College, Warsak Road Peshawar. The data was entered and analyzed in IBM SPSS software package version 23. Descriptive statistics were used to analyze gender, malaria parasites, and platelet counts. A paired sample t-test was used to analyze platelet counts. A p-value of <0.05 was considered statistically significant.

Results

Out of the total 201 cases which were included in this study, 108 (53.7%) were males, and 93 (46.3%) were females. 189 (94%) cases were suffering from Plasmodium vivax, 10 (5%) were suffering from Plasmodium falciparum, and cases infected with both P. vivax, and P. falciparum were only 2 (1%). Thrombocytopenia was present in 183 (91.04%) cases (95% confidence interval 2.13-2.37). Among the 183 cases with thrombocytopenia, 96 (52.45%) were males, and 84 (45.9%) were females. P. vivax was as likely associated with thrombocytopenia as P. falciparum (Table 1). 91.53% (n=173) of cases diagnosed with vivax had thrombocytopenia while 90% (n=9) cases diagnosed with P. falciparum had thrombocytopenia. Platelet counts on the third day started to improve, as seen in Table 2. The p-value of platelet count before and after treatment was <0.05, as seen in Table 3. Similarly, the p-value of platelet count before treatment and 3rd day of treatment was highly significant (<0.005) and the p-value of platelet count between 3rd day and after treatment was also <0.005.

Table 1: Thrombocytopenia with Malarial Parasites on Day 0

	<50,000	**50,000-99,000**	**100,000-150,000**	**>150,000**	**Total**
P. vivax	39 (20.6%)	82 (43.4%)	52 (27.5%)	16 (8.5%)	189 (100%)
P. falciparum	3 (30%)	3 (30%)	3 (30%)	1 (10%)	10 (100%)
Both	0 (0%)	0 (0%)	1 (50%)	1 (50%)	2 (100%)
Total	42 (20.9%)	85 (42.3%)	56 (27.9%)	18 (9%)	201 (100%)

Table 2: Thrombocytopenia with Malarial parasites on Day 3

	<50,000	**50,000-99,000**	**100,000-150,000**	**>150,000**	**Total**
P. vivax	9 (4.8%)	97 (51.3%)	55 (29.1%)	28 (14.8%)	189 (100%)
P. falciparum	0 (0%)	5 (50%)	3 (30%)	2 (20%)	10 (100%)
Both	0 (0%)	0 (0%)	1 (50%)	1 (50%)	2 (100%)
Total	9 (4.5%)	102 (50.7%)	59 (29.4%)	31 (15.4%)	201 (100%)

Table 3: Comparison between Platelet counts before, during, and after treatment

	Mean	N	Standard Deviation	P-Value
Platelets before treatment	88169.1542	201	43323.9108	<0.05
Platelets after 15 days at follow-up	226512.935	201	42561.9270	
Platelets before treatment	88169.1542	201	43323.9108	<0.001
Platelets on 3rd day of treatment	15753.731	201	43249.7433	
Platelets on 3rd day of treatment	105753.731	201	43249.7433	<0.001
Platelets after 15 days at follow-up	225612.935	201	42561.9270	

Discussion

In this study males (n=108, 53.7%) were infected more than females (n=93, 46.3%). Similar results were also found in a study conducted in the Larkana district of Sindh, which also found that males were infected more than females[18]. Another study conducted in district Buner also found out that males had a high incidence rate than females, which goes in favor of our study. Males had a percentage of 68.9%, and females had a percentage of 31.09%.[19]

According to a malariometric population survey, P. falciparum had a high prevalence than P. vivax in the province of Khyber Pakhtunkhwa at 10% and 8%, respectively.[8] Our results demonstrated that the infection with P. vivax was more than P. falciparum (94% vs. 5%, respectively). 1% percent of the total individuals had mixed infection with both P. vivax and P. falciparum. According to Khan et al.[20], out of the total individuals that were investigated for malaria, 17.35% were found to be positive for malarial parasite; P. vivax was 91.53%, 7.47% were infected with P. falciparum while patients that were infected with both the species were <1%. The results of this study are very close to our study. Similar results were also achieved by another study that was conducted in the Larkana district of Sindh, and they also determined that P. vivax infection was more than P. falciparum.[18]

Out of the total 201 cases, thrombocytopenia was present in 91.04% of cases (n=183). Among these, males (n=96, 52.45%) had a high incidence of thrombocytopenia than females (n=84, 45.9%). Assorted contraptions are hypothesized for thrombocytopenia in malaria, such as platelet aggregation, oxidative stress, splenic sequestration, and antibody-mediated destruction[(12)]. Contrary to a widespread belief, P. vivax gives rise to thrombocytopenia[21], as was seen in this study. 91.53% of patients suffering from P. vivax had thrombocytopenia and 90% in patients with P. falciparum. Thrombocytopenia was detected in both the patient groups infected with either P. vivax or P. falciparum, as well as in patients having both infections. Similar findings were noted in a study conducted by Erhart et al. from western Thailand.[22] Another study that was conducted in India on the relationship of thrombocytopenia with malarial species also yielded similar results. They described thrombocytopenia in both P. vivax and P. falciparum but severe thrombocytopenia was more consistent with the latter.[23] Contrary to this, our study yielded results that showed that patients infected with P. vivax had severe thrombocytopenia than patients infected with P. falciparum.

In this study, patients with thrombocytopenia on day 0 (before initiation of treatment) were 182 (90.54%) of the total 201 cases. Patients diagnosed with P. vivax and thrombocytopenia were 173 (91.53%) out of the total diagnosed with P. vivax (n=183) and those diagnosed with P. falciparum and thrombocytopenia were 9 (90%) out of the total diagnosed with P. falciparum (n=10). Patients having severe thrombocytopenia were 42 (20.9%) out of the total 201 cases. Those having moderate thrombocytopenia were 85 (42.3%), while patients having moderate thrombocytopenia were 56 (27.9%) out of the total 201 cases diagnosed with malaria. The results of our study are parallel to few other studies, which also concluded that patients suffering from malaria showed some extent of thrombocytopenia, and thrombocytopenia is

more prominent in the initial period of disease before the initiation of treatment.[24,25]

Platelet counts were repeated on 3rd day after initiation of treatment. Improvement was seen in the platelet counts of patients. Only 4.6% (n=9) patients had severe thrombocytopenia in comparison to day 0. Similarly, 50.7% (n=102) patients had moderate thrombocytopenia while 29.4% (n=59) patients had mild thrombocytopenia. Similar results were achieved by other studies in this regard as well; they discovered that with the initiation of treatment, the meantime for the disappearance of malarial parasite from the blood was 3-4 days.[26]

Conclusion

We conclude from this study that thrombocytopenia occurs in all species of malaria and is not a distinguishing attribute between the different types of malaria. With prompt identification and management, platelets count reverts back to normal.

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