Original Research Article

Study of incidence and severity of thrombocytopenia in childhood malaria and response to antimalarial therapy in a tertiary care hospital

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Abstract

Background: Malaria is a significant cause of morbidity and mortality all over world and India contributes a significant proportion of disease. There is relative paucity of data in children regarding incidence of thrombocytopenia, its severity, clinical manifestations and response to anti-malarial treatment. **Materials and methods:** The study conducted in a tertiary care hospital in south Rajasthan in over a period of one year includes 168 children less than 16 years with diagnosed case of malaria. Data were collected according to the medical records observation technique. **Results:** We found significant association of thrombocytopenia in malaria. Majority of cases with thrombocytopenia were plasmodium vivax positive, range of platelet count was 16000/cumm to 3.2lacs/cumm. Despite severe thrombocytopenia, no child had bleeding manifestations and response to treatment was significant and platelet transfusion was given to none. **Conclusion:** Thrombocytopenia in a febrile child in endemic zones should alert the physician towards the possibility of malaria. Moreover even in cases of severe thrombocytopenia, one should not panic and shouldgive anti-malarial and appropriate supportive therapy as bleeding manifestations are rare and response to therapy is good.

Keywords: Antimalarial, Malaria, Thrombocytopenia

Introduction

Despite various measures and widespread programs to control vector borne diseases, malaria still continues a major health problem affecting mankind. According to WHO malaria report, in 2016 there were an estimated 216 million case of malaria, an increase of about 5 million cases over 2015. deaths reached 445000, a similar number to previous year [1]. India contributed to about 75% of total malaria burden in Southeast Asia region.

There are five species of malarial parasite plasmodium namely *vivax, falciparum, malariae, ovale* and *knowlesi*. In India majority of infections are caused by plasmodium *vivax* and *falciparum* either individually or in a mixed fashion. Malaria starts with bite of female anopheles mosquito and parasite plasmodium infects red blood cells and affects white blood cells and platelets as well [2]. These hematological changes are most common complications and play a major role in its pathology [3]. Thrombocytopenia caused by malaria is usually mild to moderate and can be used as an indicator of malaria in febrile patients in endemic areas [4]. Incidence of thrombocytopenia in malaria has been reported to be ranging from 60%-80% in different studies with somewhat lower incidence in case of *vivax*infection [3,5].

In past plasmodium *vivax* was regarded mostly as benign but it frequently recurs and its propensity to cause severe disease is now well recognized. In different studies, it has been observed that despite severe thrombocytopenia, bleeding manifestations and requirement of platelet transfusion are rare in malaria induced thrombocytopenia [2, 4]. Because of paucity of such studies in pediatric population, we conducted this study at a tertiary care hospital in tribal area of Rajasthan to see the incidence and severity of thrombocytopenia and time taken in days for platelet count to normalize after treatment.

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Material and Methods

Place and type of study- This prospective observational study was conducted at Pacific Institute of Medical Sciences, Udaipur from 01 April 2017 to 31 March 2018.

Inclusion criteria- Children aged between 0 to 16 years admitted with fever and diagnosed as malaria were included in study.

Exclusion criteria- All case of known bleeding disorder, hematologic malignancies, immune thrombocytopenic purpura, Dengue fever and chronic liver disease were excluded from study.

Sampling methods and laboratory analysis- Diagnosis of malaria was established by peripheral blood smear which is considered as gold standard for this. Peripheral smears for malarial parasites were examined by pathologists and platelet counts were taken from automated cell counter machine.

Statistical methods- On the basis of platelet count, patients were divided into four groups. Patients with platelet count more than 1.5 lacs were normal, counts between 1.5 to 1 lac were mild, counts between 50,000 to 1 lac were moderate and platelet count below 50,000 were labeled to have severe thrombocytopenia. All case of known bleeding disorder, hematologic malignancies, immune thrombocytopenic purpura and chronic liver disease were excluded from study. Data were analyzed using SPSS Version 16.

Patients were treated with chloroquine/Artemisinin combined therapy as per standard protocol based on their clinical condition and parasite species involved. Platelet counts were taken at the time of admission and then every other day till day ten.

Results

During study period, we found a total of 168 patients who were smear positive for malaria. Out of these patients total 103(61.3%) were male and 65(38.6%) were female. Maximum patients were in 13-16 years age group (35.7%). The age and sex distribution of patients were as follows.

Table-1: Age and sex distribution of patients with malaria.

Age group	Male	Female	Total
0-4 years	7(4.1)	6(3.5)	13(7.7)
5-8 years	29(17.2)	20(11.9)	49(29.1)
9-12 years	30(17.8)	16(9.5)	46(27.3)
13-16 years	37(22)	23(13.6)	60(35.7)
Total	**103(61.3)**	**65(38.6)**	**168**

Thrombocytopenia was seen in 121(72%) patients. Severity and species wise distribution of platelet count is shown in table 2.

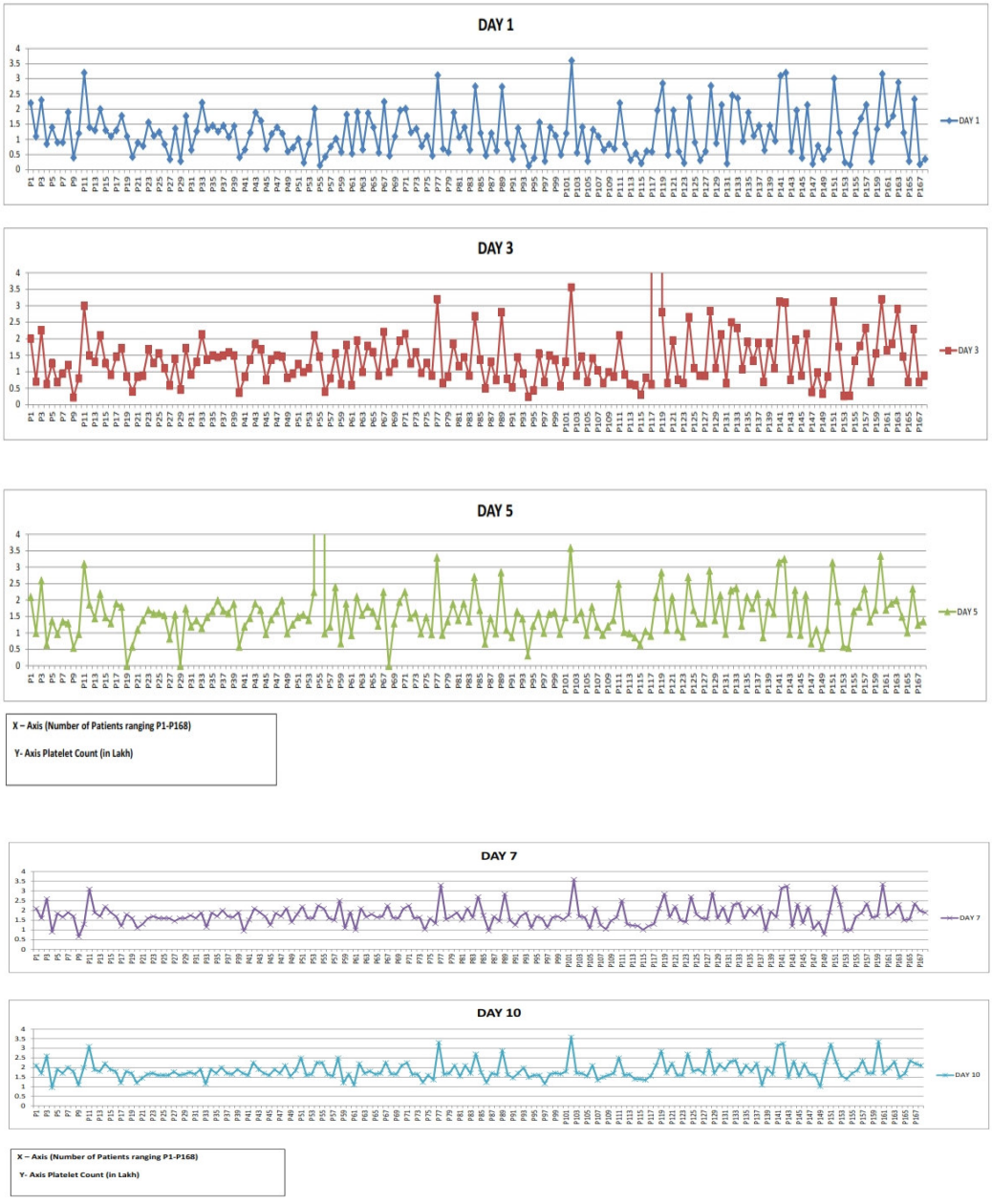
Table-2: Platelet counts in different species of malaria.

Species	Normal(>150000)	Mild(150000 - 100000)	Moderate(100000-50,000)	Severe(<50,000)	Total
Plasmodium vivax	32(19%)	28(16.6%)	22(13%)	21(12.5%)	103(61.3%)
Plasmodium falciparum	14(8.3%)	16(9.5%)	15(8.9%)	6(4.1%)	51(30.3%)
Mixed infection	2(1.1%)	6(3.5%)	4(2.3%)	2(1.1%)	14(8.3%)
	48(28.5)	50(29.7)	41(24.4)	29(17.2)	168

Platelet counts range from 16000/dl to3.2lac/dl with lowest count being observed in mixed infection. In our study of 168 patients, 103(61.3%) patients were *vivax* positive, 51(30.3%) were *falciparum* positive and 14(8.3%) were positive for mixed infection. Out of 103 patients of*vivax* malaria, 21(12.5%) had severe thrombocytopenia, 22(13.0%) had moderate and 28(16.6%) had mild thrombocytopenia. In *falciparum* positive patients, 6(4.1%) had severe thrombocytopenia, 15(8.9%) had moderate and 16(9.5%) had mild thrombocytopenia. In mixed infection patients, 2(1.1%) had severe, 4(2.3%) had moderate and 2(1.1%) patients had mild thrombocytopenia.

Out of 121 patients who had thrombocytopenia (less than150000 /cumm), 20 patients responded to anti-malarial therapy with increase in platelet count within 3 days, 26 patients responded within 5 days and 46 in 7 days. 29 Patients had persistent thrombocytopenia even after seven days. None of our patient had bleeding manifestations and no platelet transfusions weregiven.

Variation in platelet counts after initiation of anti-malarial therapy is graphically represented which show trend of improving platelets count immediately after Antimalarial treatment. On day 1 maximum number of patients in each group was having platelet count below 1.5 L. after initiation of treatment counts improved and return to normal range.



Discussion

In many parts of India, malaria is endemic and Southwest Rajasthan is in high risk zone and here incidence in children is higher [6]. Malaria affects many organs/systems in body with primary system involved is hematological. In children symptoms are more varied and often resembles to other common childhood illness, particularly gastroenteritis, meningitis/encephalitis, or pneumonia. Fever is the main symptom, but the

characteristic regular tertian and quartan patterns are rarely observed. Anemia and thrombocytopenia are highly helpful in predicting malarial infection when used in combination in febrile patients in endemic areas [7]. In Plasmodium falciparum and Plasmodium vivax malaria thrombocytopenia of varying magnitude, usually without hemorrhagic manifestations, is commonly observed. However, severe thrombo-cytopenia associated with bleeding manifestations in malarial infection is distinctly unusual [8].

In our study 74.4% patients were found to have thrombocytopenia most of which were from plasmodium *vivax* group. In one large study done by Tanwar GS et al involving 676 cases from Bikaner, Rajasthan, incidence was 65.38% [9]. In a study in Delhi by Meena et al and in Mangalore by Fassela et alfound similar results with a percentage of 70% and 82% respectively [5, 10].

Incidence of thrombocytopenia in different species of malaria is 68.9% in *vivax*, 72.5%in *falciparum* and 85% in mixed infection cases. In a study from north India in a pediatric hospital, they found 40%, 52%and 50%in*vivax*, *falciparum* and mixed infections respectively [11]. In a study from Bikaner similar results were found for falciparum (55.3%) and mixed infection (55.8%) but higher for *vivax* (73%)[9]. Our results for thrombocytopenia in *falciparum* and *vivax* case are comparable with study by Horstmann et al [12]. Bleeding manifestations were not seen in any of our patients and platelet transfusions were given to none. Similar findings were noted in other studies also by Latif et al, Omar et al and Maina et al [4, 11, and 13]. In our study patients responded well to antimalarial therapy with subsidence of feverand increase in platelet count gradually. This is similar to results obtained in other studies by Latif et al and Gonzalez et al [4, 14].

The exact mechanisms underlying the reduction in platelet counts is still not known, but various hypothesis have been advanced including immune-mediated phenomena, oxidative stress, alterations in splenic function and a direct interaction between the parasite and platelets [15.16.17,18]. Recently, Coelho and coworkers demonstrated that macrophage-driven phagocytosis of platelets may be an important contributory mechanism and that the mean platelet volume was greater in thrombocytopenic patients with vivax malaria than in controls [19]. The latter finding is particularly interesting because the presence of large circulating platelets and may be viewed as compensatory mechanism in order to preserve primary hemostasis.

Thrombocytopenia in malaria is well tolerated and this can be explained by enhance aggregability and platelet activation [20]. Hypersensitive platelets following malarial infection which enhance haemostatic response have also been suggested as a reason of low incidence of bleeding despite thrombocytopenia in malaria [20, 21]. Moulin and others reported that thrombocytopenia was not a marker of severity in children suffering falciparum malaria [22].

Conclusion

Thrombocytopenia in a febrile child in endemic zones should alert the physician towardsthe possibility of malaria.

What this study add to existing knowledge- Moreover even in cases of severe thrombocytopenia, one should not panic and should give antimalarial and appropriate supportive therapy as bleedingmanifestation are rare and response to therapy is good.

Contribution by different authors: All authors contributed in this research work and formation of this manuscript. GD performed the clinical assessments, data collection and drafted the manuscript. GD and VP treated the patient in the inpatient department. VP, SB and RK searched the literature and drafted manuscript.

SB confirmed the laboratory reports. VP and RK treated the patient until discharge and drafted the manuscript. RK and SB did the data analysis and statistical work. All authors read and approved the final manuscript.

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