Platelet Count – A Diagnostic Aid In Fever

Dr. Himanshu A. Joshi*, Dr. Seema S. Shah**

*Associate Prof. In Pediatrics, ** Assistant Prof. In Pediatrics, GMERS Medical College, Gandhinagar.

Abstract : Introduction: Vivax Malarial infection. Dengue Viral fever is also emerging as a Febrile conditions to have reduced platelet count. The absence of the normal platelet count on peripheral smear in case of fever is a clue to the presence of Malaria and Dengue fever. Material & Method: Present study we have tried to study the pattern of thrombocytopenia in these febrile conditions and their diagnostic and prognostic implications. The study was conducted at GMERs Medical College, Gandhinagar. This study group consisted of 146 Patients of Fever treated at Pediatric Department, Malaria diagnosed by thick & thin smear examination. The platelet count was done by Abascus Junior B- Blood Cell counter. Dengue Fever was diagnosed by NS1 Antigen Test. The Mean Platelet counts in P. Falciparum are 69852 cells/mm3, P.Vivax 1,15,580 and Dengue Fever 53,100. Statistically the difference between P. Falciparum & Vivax is significant for differentiating Malarial type. Result: Platelet count <20,0000 cells/mm^3 was observed in both the types of Malaria and not seen with Dengue Fever. Profound thrombocytopenia still remains the distinguishing, feature of P. Falciparum Malaria. Platelet count more than 1,00,000 cells/mm^3 favours the diagnosis of P.Vivax & Moderate reduction in Platelet Count (between 20,000 to 1,00,00) is clue to P. Falciparum and Dengue Fever. In this segment other diagnostic criteria like pFHrp Antigen and N.S.Antigen should be applied to differentiate these two grave conditions. Thrombocytopenia (Platelet count <150000 cells/mm^3) can be considered as a predictor of Malaria and in combination with Anemia (Hb<10gm/dl) is a next best parameter. Unlike Malaria, in Dengue fever thrombocytopenia is usually associated with normal Hemoglobin. [Joshi H et al NJIRM 2013; 4(3) : 128-132]
Key Words: Plasmodium Vivax Malaria, P.Falciparum Malaria, Dengue Fever, Thrombocytopenia.

Author for correspondence: Dr. Himanshu A. Joshi, Associate Prof. In Pediatrics, GMERS Medical College, Gandhinagar. E- mail: drhimanshu.joshi60@gmail.com;

Introduction: Clinical diagnosis, the most widely used approach for diagnosis of Malaria in tropics, is unreliable because the clinical presentation of Malaria is diverse and in a tropical country, it may be difficult to distinguish from Viral Fever & Typhoid Fever. Clinical diagnosis is only accurate in 50% of cases of Malaria. The examination of thick & thin blood smear under light microscope is the gold standard in the diagnosis of Malaria. It is informative and inexpensive but it requires expertise and repeated smear examinations.. Thrombocytopenia is commonly associated with[1] Plasmodium Facliparum Malaria and rarely with Plasmodium Vivax Malaria[2] Various hematologic abnormalities have been reported with Malaria[3,4] Dengue Viral fever is now a days emerging with thrombocytopenia. In the present series we have tried to study the Hematologic Parameters like thrombocytopenia and Anaemia in cases of Fever and their Diagnostic Implications. Fortunately many cases were associated with severe thrombocytopenia but not associated with clinically evident bleeding.

Material And Methods : From April 2011 to January 2012, a total number of 146 patients with Fever, in Paediatric Department at GMERS Medical College, Gandhinagar were taken for study in this series. The commonest manifestations of the patients were fever with rigours, bodyache, headache and febrile convulsions. The diagnosis was based on the gold standard thick and thin blood smear examination with external quality control. Special precautions were taken to differentiate P. Falciparum and Vivax Malaria as well as mixed infection. The platelet count were done by Abacus Junior – B Blood Cell Counter. The diagnosis of dengue fever was confirmed by N.S.1 Antigen test.

Results : In P. Vivax Malaria Platelet count less than 1,50,000 cells.mm^3 was noted in 73.74% patients. The mean platelet count in was 1,15,580 cells/mm^3 SD $\pm$ 91334 and with a range of 18,000 cell/mm^3 to 5,10,000 cells/mm^3. The lowest platelet count was 18000 cells/mm^3.

Platelet count less than 1,50,000 cells/mm3 was observed in 81.7%. Patients P Falciparum Malaria ranging from 9,000 to 2,10,000 cells/mm^3 with mean of 69852 cells/mm^3 SD ± 53017. The lowest platelet count was 9000 cells/mm^3.

The mean Platelet count in Dengue fever is 53100 cells/mm³ SD ± 32814. Ranging from 32000 to 88000 cells/mm³.

Plasmodium Vivax Malaria

Platelet Count	<20,000 Cells /mm³ A	20,000 to 50,000 Cells /mm³ B	50,000 to 1,50,000 Cells /mm³ C	>1,50,000 Cells /mm³ D
No. of Patients	2	27	44	26
%	2.12	27.27	44.56	26.26

P. Falciparum Malaria

Platelet Count	<20,000 Cells /mm³ A	20,000 to 50,000 Cells /mm³ B	50,000 to 1,50,000 Cells /mm³ C	>1,50,000 Cells /mm³ D
No. of Patients	4	14	13	5
%	11.11	38.88	36.11	13.9

Dengue Fever

Platelet Count	<20,000 Cells /mm³ A	20,000 to 50,000 Cells /mm³ B	50,000 to 1,50,000 Cells /mm³ C
No. of Patients	-	5	6
%	-	45.45	54.54

Platelet count less than 20000 cell/mm³ was observed in only 2.07% patients in P.Vivax Malaria while it was in 11.1 patients of Falciparum Malaria.

Platelet count ranging from 20,000 cells/mm³ to 50000 cell/mm³ was observed in 27.27% patients of P.Vivax Malaria 38.88% in Falciparum Malaria & 45.45% patients of Dengue Fever.

Platelet count ranging from 50,000 to 1,50,000 cells/mm³ was noted in 44.56% patients of Vivax Malaria, 36.11% in Falciparum Malaria and 54.54% in Dengue Fever.

Normal Platelet count was noted in 26.26% patients of Vivax Malaria and 13.9% in Falciparum Malaria.

The hemoglobin level also altered in the P Vivax Malarial infection. Mean Hemoglobin level with the subjects of P.Vivax Malaria and thrombocytopenia was 8.87 gm/dl. while the mean hemoglobin level was 11.8 gm/dl in patients with normal platelet count. The mean hemoglobin level with Falciparum Malaria with low platelet with count patient was 8.61 gm/dl. & Dengue Fever 11.8 gm/dl.

None of the subjects with low platelet count had clinical manifestation of thrombocytopenia or bleeding from any site and platelet transfusion was not required.

Discussion : Malaria remains today one of the major health problems in the tropics with increased morbidity and mortality. Falciparum Malaria presents with protean manifestations and is usually associated with a variety of complications and has a high mortality. Plamodium Falciparum, in contrast to the benign malarias, may progress to a life threatening multisystem disease. The global case fatality rate of Falciparum infection is around 2 million deaths per year.

Thrombocytopenia is a common feature of Acute Malaria and is observed in both P. Falciparum & P.Vivax infection regardless of the seventy of infection. The absence of the normal quantity of platelets on a peripheral smear in a case of fever is often a clue to the presence of Malaria and Dengue viral fever. Thrombocytopenia is accompanied by clinical bleeding or Biochemical evidence of DIC.

Platelet count can fall below 20000 cells/mm³ but it is less common. In this study platelet count <20,000 cells/mm³ was observed in 2.02% in P.Vivax infection while it is reported in 11.11% cases of P.Falciparum Malaria. Dengue Fever is not having such a low thrombocytopenia, Hence platelet count <20,000 or severe thrombocytopenia may be kept as a clue to suggest Falciparum Malaria, other studies & reports of V M Jadhav in JAPI also observed the same.[5] Early initiation of treatment in such cases may prevent complications and mortality.

Thrombocytopenia is less reported in P.Vivax Malaria & considered to be common with P. Falciparum Malaria. In our study the platelet count from 20,000 to 1,50,000 range was in 74.99% of cases of P. Falciparum Malaria and 71.81% patients with P. Vivax Malaria. A similar observation was noticed in one study in which thrombocytopenia was seen in 85% of patients with Vivax & Malaria & in all the patients with severe Facliparum Malaria.[6] This strikingly low platelet count in P.Vivax Malaria confuses the differentiate diagnosis with P. Falciparum & Dengue viral fever. As the severity, course of disease, treatment & prognosis varies with each fever it is crucial to differential such conditions. The use of pFHrp Antigen test for Falciparum Malaria may be recommended, particularly in cases where peripheral smear is negative for Malarial Parasite. This parasight F Antigen capture assay (Dipstick test) is based on detection of circulating histadine rich protein 2 Antigen. The sensitivity of this test is 87% similar to that of Microscopy 83%. The Dipstick test is accurate & sensitive in low. Parasitemia upto 50 parasites /microliter.

The mean Platelet count in the P.Vivax is 1,15,580 cell/mm^3 while in Falciparum Malaria it is 69850 SD ± 53017. This suggests that there is statistically significant difference in the prevalence of thrombocytopenia between two types of Malaria. Similar observations were noticed in a study by v.jadhav in which mean platelet counts in P.Vivax & Falciparum Malaria were 1,15,390 cells/mm^3 & 1,00,900 cells/mm^3 respectively.[7] This Finding can be helpful in distinguishing the type of Malaria up to certain extent.

Profound thrombocytopenia with platelet count as low as 5000 cells/mm3 is frequently reported with Falciparum Malaria, but only one case is found in Indian Literature in a female patient of Vivax Malaria.[8] In our study lowest platelet counts in case of P. Falciparum is 9,000 cells/mm^3 and 18,000 cells/mm^3 in P.Vivax Malaria. All patients with both types of Malaria having platelet count <20,000 did not had clinically evident bleeding and platelet transfusion was not required. This suggest that this low platelet count can be transient in the course of Malarial disease conditions and not

necessarily have prognostic implications. Platelet Transfusion is indicated only in the patients with systemic bleeding. Considering these facts we may avoid unnecessary platelet Transfusions in Profound Thrombocytopenia with malaria.

As shown in the table thrombocytopenia with Dengue Fever is not as profound as P. Falciparum Malaria. Platelet count <20,000 cells/mm^3 was not reported in patients of Dengue Fever. The mean platelet count is 53,100 cells/mm^3, that is lower than the mean platelet count of P.Falciparum Malaria. All patients of Dengue had thrombocytopenia ranging from 32,000 cells/mm^3 to 88,000 cells/mm^3. In this range of platelet count maximum patients (74.99%) of P. Falciparum Malaria are also observed. Hence, in this segment of thrombocytopenia with fever in which peripheral smear is not confirmatory of Malaria. Dengue antigen and IgG, IgM estimation is necessary to distinguish life threatening conditions like Falciparum Malaria & Dengue Fever.

The mean hemoglobin levels in the patients with P.Vivax & P. Faciparum with thrombocytopenia are 8.87 & 8.61 gm/dl respectively. This value is significantly lower than the patients with Malaria with normal platelet count. The similar observations were noticed by Lathi T.B in their study.[9] Low platelet count <15,000 cells/mm3 was 60% sensitive and 88% specific for the Diagnosis of Malaria. This was the only descreminator parameter with positive and negative likelihood ratio of 5.04 and 0.45 respectively. The combination of Anaemia (Hb <10 gm/dl) and thrombocytopenia had higher sensitivity 69% and positive likelihood ratio of 2.77. These parameters were used as an Index Test. It is observed that children having combination of Thrombocytopenia and Anemia are 22 times more likely to have Malaria then the children without combination.

All the patient with Dengue fever has thrombocytopenia in the range of 32,000 cells/mm^3 to 88,000 cells/mm^3 and mean hemoglobin level was 11.8 gm/dl. This result may be of greater help in differentiating the condition like Malaria in which Hemoglobin levels are significantly decreased. Al Fanso & Morales also reports the same in their study.[10]

The exact mechanism for thrombocytopenia in Malaria is not known. Various theories are suggested. It can be direct lytic effect of the parasites on the platelet [11].

Oxidative stress damage of thrombocytopenia has also been implicated in the etiopathogeneric of thrombocytopenia in Malaria [12] (Evel O, Akosyn N). It can be a result of combination of hemolytic mechanism and accelerated removal of both parasitized and non parasitized red blood cells with depressed and ineffective erythropoiesis.

Conclusion : A variety of Hematological alterations have been reported in Malaria by various studies as blood counts are now readily available with the use of Automated Analyzer. Absence of Thrombocytopenia is uncommon in the laboratory diagnosis of Malaria. Presence of thrombocytopenia is not a distinguishing feature between two types of Malaria and Dengue Fever. Thrombocytopenia now a days is frequently observed feature of P.Vivax Malaria. As seen in this study and study by V.M.Jadhav that Thrombocytopenia in P.Vivax Malaria is having mean value near 1,15,580 cells/mm^3, & can be considered as mild thrombocytopenia. The mean Platelet count in Falciparum Malaria is 69850 cells/mm3 SD ± 53017, which significantly lower than thrombocytopenia of P.Vivax Malaria. This observation may be considered as differentiating feature between two types of malaria.

Platelet count <50,000 cells/mm^3 is less common with P.Vivax Malaria (29.34%) but it is reported to be 50% in patients of Falciparum Malaria. Thrombocytopenia <20,000 cells/mm3 requires a due attention. Statistically it is more reported with Falciparum Malaria. Hence we can conclude that profound thrombocytopenia can be suggestive of Falciparum Malaria probably due to high parasitemia. Rapid fall in hemoglobin (severe Anemia) with this type of Malaria confirms the diagnosis of Falciparum Malaria because of severe hemolysis due to high parastienia. The degree of anaemia correlates with Parasitenia & Schizontenia.

In Dengue Viral Fever platelet count range was 50,000 to 1,50,000 cells/mm^3. All the patients had thrombocytopenia, but platelet count < 20,000 cells/mm^3 was not reported. Hence Febrile conditions with Platelet count in this range requires more attention to differentiate from Falciparum Malaria as here Platelet Count remains in this same range. Both the conditions have grave course of disease and complications are more. Use of pFHrp (Dipstick) test for Falciparum Malaria and NS Antigen Test for dengue fever may be of great help to differentiate this condition and prevent complication and mortality.

Result confirms that Hematological Abnormalities like thrombocytopenia & Anaemia are hall mark if malarial infection. Thrombocytopenia (Platelet count <15,000 cells/mm^3 can be a predictor of Malarial Disease and in combination with Anaemia (Hb <10 gm/dl) would work as a next best parameter. Thrombocytopenia with unaltered hemoglobin levels can be suggestive of Viral fevers like Dengue.

This thrombocytopenia disappears with the treatment of the disease and required no specific treatment for itself.

Further study in Malaria establishing the relationship between severity of Thrombocytopenia with Hemoglobin levels (Anaemia) and Formulation of Index Test would be of emmance help in management of the disease particularly when peripheral smear is negative for parasites.

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