www.jmscr.igmpublication.org Impact Factor 3.79
ISSN (e)-2347-176x

IGM Publication Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Throbocytopenia an Indicator of Malaria in Febrile Patients- A Retrospective Study

Authors
Vissa Shanthi MD[1], Swathi Sreesailam M.D[2], Nandam Mohan Rao MD[3], Shyam Sundara Rao M.D[4], Bhavana Grandhi M.D[5]
[1]Associate Professor, Department of pathology Narayana Medical college and Hospital, Nellore, Andhrapradesh, India.
Email: *santhijp@gmail.com*
[2]Assistant Professor, Department of Pathology, Narayana Medical College and hospital Nellore, Andhrapradesh, India
Email: *swathi191083@gmail.com*
[3]Associate Professor, Department of pathology, Narayana Medical college and hospital, Nellore, Andhrapradesh, India.
Email: *nmr2020kmc@gmail.com*
[4]Associate Professor, Department of Pathology, Narayana Medical College and hospital Nellore, Andhrapradesh, India
Email: *syam.byna@gmail.com*
[5]Assistant Professor, Department of Pathology, Narayana Medical College and hospital Nellore, Andhrapradesh, India
Email: *drbhavanagrandhi@gmail.com*
Corresponding Author
Dr. V. Shanthi
Flat no. 301, Anjani SVGK Towers, Sri Hari nagar, Ramalingapuram, Nellore, Andhra Pradesh, India
Email: *santhijp@gmail.com,* Phone - +91-9849052179

Abstract

Back ground: *Malaria is a major health problem in India. It is mosquitoe born protozoal disease caused by parasite of the genus Plasmodium. Various hematological consequences are produced in patients with this infection, out of which thrombocytopenia is the most common.*

Objective*: To analyze thrombocytopenia and its severity in patients infected with malarial parasite.*

Methods: *The prospective study was conducted during the period of November 2013 to December 2014 on 204 patients who were malaria infected. The diagnosis of malaria was done by peripheral smear examination. Platelet count were performed using automated cell counter. Thrombocytopenia was categorized into mild (1,00,000 – 1,50,000/µl), moderate (1,00,000 – 50,000/µl) and severe (less than 50,000/µl). Presence and severity of thrombocytopenia was compared in different types of malaria.*

Results: *In the study group of 204 malaria infected patients, males were 148 (72.55%) and females were 56 (27.45%). In these patients vivax infection was predominant (76.47%) when compared to falciparum (19.61%) infection and mixed infections (3.92%). The analysis of thrombocytopenias in these patients showed that both the vivax and falciparum infected patients had moderate thrombocytopenia in majority cases. Patients with mixed infection showed moderate and severe thrombocytopenia and no case with mixed infection had normal platelet count in these patients.*

Conclusion: *Presence of thrombocytopenia in patients with fever and chills acts as an indicator of malaria infection, though the severity of the thrombocytopenia is not useful for distinguishing the types of malaria.*

Key words: *Plasmodium, Peripheral smear, Thrombocytopenia*

Introduction

Malaria is a major public health problem caused by the infection with protozoan parasite of the genus Plasmodium. In humans malaria is caused by 5 species of Plasmodium (i,e. Plasmodium vivax, P.falciparum, P.malariae, P.ovale, P. knowlesi). About 243 million malaria cases were recorded worldwide in 2008. Nearly 85% of cases were in African region, which was followed by South-East Asian region (10%) and East mediterranean region (4%). Approximately 8,63,000 deaths were estimated to be due to malaria[(1)] .

In India 1.52 million malaria cases were recorded, out of which Plasmodium falciparum was responsible for 50% of cases. Malaria was responsible for 924 deaths[(2)]. Morbidity and mortality due to malarial infection can be reduced by early diagnosis and effective treatment. Many sensitive methods like Polymerase Chain Reaction and malaria antigen-based rapid diagnostic tests are available, but they are expensive. Light microscopic examination of thin and thick blood films is informative and inexpensive though it requires expertise and repeated smear examination [(3)] .

Various hematological changes are seen in the patients with malarial infection, out of which thrombocytopenia is most common[(4)]. Careful search for malarial parasite should be done in patients with thrombocytopenia. Our study was done to correlate the presence and severity of thrombocytopenia with types of malaria.

Material and methods

The prospective study was conducted in Narayana Medical College and Hospital for a period of 14 months i,e. November 2013 to Decmber 2014. Patients of all ages with malarial infection who attended OPD and hospitalized were included in our study. Malarial infection was confirmed by the examination of peripheral smear which was stained by Leishman stain. Complete blood counts of these patients were noted by using automated Hematology analyzer. Depending upon the platelet count thrombocytopenias were divided into 3 subgroups. Thrombocytopenia was considered to be mild if the platelet count is between 1,00,000 to 1,50,000/µl, moderate if between 1,00,000 to 50,000/µl and severe if less

than 50,000/µl. Platelet count was correlated with types of Plasmodium causing malarial infection.

Results

Our study included 204 malaria positive patients. Out of 204 patients 148 (72.55%) were males and 56 (27.45%) were females. All the patients were between 1 year to 75 years with maximum number of patients between 21 to 45 years (Table-1).

In the study group of 204 patients, 156 (76.47%) were positive for P.vivax, 40 (19.61%) were positive for P.falciparum and 8 (3.92%) had mixed infections. This showed the prevalence of P.vivax when compared to P.falciparum. Age wise distribution of cases with different malarial infection showed that maximum number of cases with P.falciparum were in the age group of 31 – 40 years and maximum number of P.vivax cases were seen in the age group of 21 – 40 years where as the cases with mixed infections were seen in the age group of 31- 50 years (Table-2).

Out of 156 cases with P.vivax, 20 cases (12.82%) had normal platelet count, 44 cases (28.21%) had mild thrombocytopenia, 48 cases (30.76%) had moderate thrombocytopenia and 44 cases (28.21%) had severe thrombocytopenia. Out of 40 cases with P.falciparum infection, 4 cases (10%) had normal platelet count, 8 cases (20%) had mild thrombocytopenia, 16 cases (40%) had moderate thrombocytopenia and 12 cases (30%) had severe thrombocytopenia. 8 cases had mixed infection, out of which 4 cases (50%) had moderate thrombocytopenia and 4 cases (50%) had severe thrombocytopenia (Table-3). This has shown that majority of cases with P.falciparum and P.vivax infection had moderate thrombocytopenia. In case of mixed infection, no case of mild thrombocytopenia and with normal platelet count were noted.

Table – 1: Age and sex wise distribution of malarial patient

Age in years	Male patient	Female patient
< 20 years	20 (13.51%)	32 (57.14%)
21 – 45 years	80 (54.05%)	24 (42.86%)
>45 years	48 (32.43)	
Total (n=204)	148 (72.55%)	56 (27.45%)

Table – 2: Age wise distribution in patients with P.falciparum, P.vivax and mixed infections

Age in years	P.falciparum	P.vivax	Mixed infections
0 – 10 years	8 (20%)	8 (5.13%)	
11 – 20 years	4 (10%)	32 (20.51%)	
21 – 30 years		36 (23.08%)	

31 – 40 years	16 (40 %)	36 (23.08%)	4 (50%)
41 – 50 years	4 (10%)	12 (7.69%)	4 (50%)
51 – 60 years	8 (20%)	4 (2.56%)	
➢ 60 years		28 (17.95%)	
Total (n=204)	40 (19.61%)	156 (76.47%)	8 (3.92%)

Table – 3: Platelet count in different malaria patients

Platelet count in µl	P.falciparum	P.vivax	Mixed infections
➢ 1,50,000	4 (10%)	20 (12.82%)	
1,50,000-1,00,000	8 (20%)	44 (28.21%)	
1,00,000-50,000	16 (40%)	48 (30.76%)	4 (50%)
< 50,000	12 (30%)	44 (28.21%)	4 (50%)
TOTAL (n=204)	40 (19.61%)	156 (76.47%)	8 (3.92%)

Table -4: Prevalence of malaria in different studies

Type of malarial infection	Manmeet K Gill et al (2013)	Our study (2015)
P.vivax	92 (76.67%)	156 (76.47%)
P.falciparum	18 (15%)	40 (19.61%)
Mixed infections	10 (8.33%)	8 (3.92%)
Total	120	204

Table – 5: Platelet count in malaria patients in different studies

Types of malaria infection	Thrombocytopenia		Normal platelet count	
	Manmeet K Gill et al (2013)	Our study (2015)	Manmeet K Gill et al (2013)	Our study (2015)
P.vivax	50 (54.35%)	136 (87.18%)	42 (45.6%)	20 (12.82%)
P.falciparum	16 (88.89%)	36 (90%)	2 (11.11%)	4 (10%)
Mixed infections	10 (100%)	8 (100%)	-	-
Total	76	180	44	24

Table – 6: Thrombocytopenia in malaria patients in different study

Platelet counts	P.vivax		P.falciparum		Mixed infections	
	Manmeet K Gill et al (2013)	Our study (2015)	Manmeet K Gill et al (2013)	Our study (2015)	Manmeet K Gill et al (2013)	Our study (2015)
➢ 1,50,000	42 (45.6%)	20 (12.82%)	2 (11.11%)	4 (10%)	-	-
1,50,000-1,00,000	16 (17.4%)	44 (28.21%)	4 (22.22%)	8 (20%)	2 (20%)	
1,00,000-50,000	18 (19.5%)	48 (30.76%)	6 (33.33%)	16 (40%)	4 (40%)	4 (50%)
< 50,000	16 (17.4%)	44 (28.21%)	6 (33.33%)	12 (30%)	4 (40%)	4 (50%)

Discussion

Malaria is a major health problem with increased morbidity and mortality and is endemic in many parts of India. 77% of the total Southeast Asian malaria cases are contributed by India[5] . In India malaria is caused by P.vivax and P.falciparum. Malarial infection causes many hematological changes, out of which thrombocytopenia is the most common hematological feature of acute malaria. The patient having fever with thrombocytopenia often gives a clue to the presence of malarial infection. After the recovery of the patients, Platelet count increases rapidly[6]. Though thrombocytopenia is noted in both P.vivax and P.falciparum malaria infection, the frequency and severity of thrombocytopenia is more among the patients having P.vivax infection[7].

Although the exact pathogenetic mechanism of thrombocytopenia in malarial patients is not fully understood, yet the possibility of involvement of multifactorial phenomenon in the destruction of platelets is considered[8]. The cause of thrombocytopenia in malaria patient can be due to activation[9] or apoptosis[10] or possibly due to immune complexes generated by malarial antigen leading to sequestration of damaged platelets in spleen which are later phagocytosed by splenic macrophages[11].

One of the cause for phagocytosis of platelets in malaria patients has been proposed to be due to increased expression of P-selectin on the surface of activated platelets[12]. It has also been proposed that thrombocytopenia is also related to release of cytokines during acute inflammatory response. Some studies have shown that in children with P.falciparum infection, thrombocytopenia is associated with increased plasma concentration of IL-10 and is not related to parasitemia or any other cytokines[13]. In the studies done by Park and colleagues, thrombocytopenia in patients with P.vivax infection was found to be related to the higher levels of IL-1, IL-6, IL-10 and TGF-β[14]. Other cytokines like IFN –γ and TNF-α were also

found to be raised and their high levels were often correlated with severity of thrombocytopenia in humans infected with P.falciparum and P.vivax[15]

In the malaria two types of platelet dysfunctions are noticed. Initially there is platelet hyperactivity followed later by hypoactivity. Certain factors like contact of platelet membrane with red cells infected by malarial parasite, damage to endothelial cells and aggregating agents like immune complexes results in hyperactivity of platelets. The platelets which are injured undergo intravascular lysis. After lysis, the contents of the platelets are released which activates the coagulation cascade and results in DIC. Following this phase there is transient platelet hypoactivity. Later platelets become active and normal in one or two weeks[16].

In our study P. vivax was found to be more prevalent than P.falciparum which coincided with studies done by Manmeet K. Gill et al[17] (2013) (Table-4). In both P.vivax and P.falciparum infections maximum patients had thrombocyto-penia. In patients with thrombocytopenias majority of cases had moderate thrombocyto-penias indicating that severity of thrombocyt-openia cannot be used to differentiate the type of malaria. Our study correlated with studies done by Manmeet K.Gill et al (2013) (Table 5 , Table-6).

This low platelet count might be transient in the course of disease which does not have much prognostic significance. Clinical bleeding manifestation are seen in less than 5-10% of severe malaria patients. Platelet concentrate transfusion is not required in malaria patients even with severe thrombocytopenia. Thrombocytopenia will be improved with the resolution of disease within a week or within 28 days [18] .

Conclusion

In the patients with acute febrile illness, the presence of thrombocytopenia should raise the suspicion of malarial infection. Simple Peripheral smear examination can give clue to the diagnosis of malaria and can help to provide the prompt treatment to the patients. However the severity of thrombocytopenia does not help to differentiate the type of malarial infection.

References

1. WHO. World Malaria Report. Geneva Switzerland: WHO Press;2009.
2. Government of India. Strategic Action Plan for malaria control in India 2007-2012,New Delhi: DGHS, Ministry of Health and Family Welfare;2009.
3. Khan SA, Ali W. Platelet count in malaria. Pak J Pathol 2008;19:86-8.
4. Khan SA, Khan FR, Usman M, Zahid S. Malaria can lead to thrombocytopenia. Rawal Med J 2008;33:183-5.
5. Faseela TS, Ronald AR, Anita KB, Chaitra SM, Rai Y. Diagnostic value of platelet count in malaria. J Clin Diagn Res 2011;5:464-6.
6. Jadhav UM, Patkar VS, Kadam NN. Thrombocytopenia in malaria – Correlation with type and severity of malaria. J Assoc Physicians India 2004;52:615-8.

7. Kochar DK, Das A, Kochar A, Middha S, Acharya J, et al. Thrombocytopenia in Plasmodium falciparum, Plasmodium vivax and mixed infection malaria: a study from Bikaner (Noorthwestern India). Platelets 2010;21:623-627.
8. Cox D, Mc Conkey S. The role of platelets in the pathogenesis of cerebral malaria. Cell Mol Life Sci 2010;67:557-568.
9. Lee SH, Looareesuwan S, Chan J, Wilairatana P, Vanijanonta S, et al. Plasma macrophage colony-stimulating factor and P-selectin levels in malaria-associated thrombocytopenia. Thromb Haemostat 1997;77:289-293.
10. Piguet PF, Kan CD, Vesin C. Thrombocytopenia in an animal model of malaria is associated with an increased caspase-mediated death of thrombocytes. Apoptosis 2002;7:91-98.
11. Yamaguchi S, Kubota T, Yamagishi J, Okamoto K, Izumi T, et al. Severe thrombocytopenia suggesting immunological mechanisms in two cases of vivax malaria. Am J Hematol 1997;56:183-186.
12. Badlou BA, Wu YP, Smid WM, Akkeman JW. Platelet binding and phagocytosis by macrophages. Transfusion 2006;46:1432-1443.
13. Casals-Pascual C, Kai O, Newton CR, Peshu N, Roberts DJ. Thrombocytopenia in falciparum malaria is associated with high concentrations of IL-10. Am J Trop Med Hyg 2006;75:434-436.
14. Park JW, Park SH, Yeom JS, Huh AJ, Cho YK, et al. Serum cytokine profiles in patients with Plasmodium vivax malaria: a comparision between those who presented with and without thrombocytopenia. Ann Trop Med Parasitol 2003;97:339-344.
15. Andrade BB, Reis- Filho A, Souza-Neto SM, Clarenicio J, Camargo LM et al. Severe Plasmodium vivax malaria exhibits marked inflammatory imbalance. Malar J 2010;9:13.
16. Srichaikul T, Pulket C, Sirisatepisan T, Prayoonwiwat W. Platelet dysfunction in malaria. Southeast Asian J Trop Med Pub Health 1988;71:832-6.
17. Manmeet K.Gill, Manisha Makkar, Sachan Bhat, Tanveer Kaur, Kalpana Jain, Geetika Dhir. Thrombocytopenia in malaria and its correlation with different types of malaria. Annals of Tropical Medicine and Public Health 2013;6(2):197-200.
18. Moulin F, Lesage F, Legros AH, Maroga C, Moussavou A, Guyon P, *et al*. Thrombocytopenia and Plasmodium falciparum malaria in children with different exposures. Arch Dis Child 2003;88 : 540-1.