

Isolated thrombocytopenia in acute malaria: association with vitamin B12 and folic acid levels

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Abstract

Background: The objective of the present study was to evaluate the association of thrombocytopenia with vitamin B12 and folic acid levels in cases of acute malaria and also to see if any difference exists between cases of falciparum and vivax malaria. **Materials and Methods:** It was a hospital based observational study including 50 patients of diagnosed malaria with thrombocytopenia presenting to the medical OPD/ IPD. The thick and thin slides were prepared according to the WHO guidelines. The platelet counts were visually confirmed by a clinical hematologist after the counts were done by an auto analyzer machine. Laboratory tests done on these patients consisted of full blood counts, liver enzymes, renal function, vitamin B12 levels, folic acid levels and erythrocyte sedimentation rate. Data was analyzed using SPSS software ver. 21. **Results:** Prevalence of low folate/ Vitamin B12 levels was 56% (Table 1). About one fourth (26%) cases had grade I thrombocytopenia while 18% and 56% had grade II and III thrombocytopenia respectively. A significant association was observed between low folate/ Vitamin B12 levels and severity of thrombocytopenia while no difference was observed between low folate/ Vitamin B12 levels and type of malaria. **Conclusion:** Vitamin B12 and folic acid deficiency is positively associated with isolated thrombocytopenia in cases of acute malaria. Thus early Vitamin B12 and folic acid supplementation might help in obviating the severity of malaria and should be given in all cases of acute malaria.


Key Words: Acute Malaria, Folic Acid, Thrombocytopenia, Vitamin B12.

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INTRODUCTION

Malaria is commonly associated with various degrees of hematological complications like anemia and thrombocytopenia. The anemia is usually due to varied reasons ranging from hemolysis to comorbidities like parasitic infections, folate, iron, and vitamin B12 deficiencies in endemic areas, anti-malarials and further complicated by the coexistence of thalassemia and other haemoglobinopathies^{1,2}. A number of observational

studies have confirmed the association of thrombocytopenia to malaria but till date the cause of thrombocytopenia is poorly understood. The speculated mechanisms leading to thrombocytopenia are coagulation disturbances, splenomegaly, bone marrow alterations, antibody-mediated platelet destruction, oxidative stress, and the role of platelets as cofactors in triggering severe malaria³⁻⁵. Some studies have also suggested that the low levels of platelets may in some instances be related to a folate or vitamin B₁₂ deficiency⁶. The present study was thus planned to study the association of thrombocytopenia with vitamin B12 and folic acid levels in cases of acute malaria and also to see if any difference exist between cases of falciparum and vivax malaria.

MATERIAL AND METHODS

Present study was a hospital based observational study conducted at a tertiary care centre and medical college of Navi Mumbai, India. A total of 50 patients of malaria (vivax/ falciparum/ mixed) with thrombocytopenia presenting to the medical OPD/ IPD were included in the

study. Patients with age less than 12 and above 60 years, those with normal platelet count (>1.5lakh/ dl) and those with other haematological abnormalities (abnormalities of RBC and WBC lineages) were excluded from the study. The thick and thin slides were prepared according to the WHO guidelines and studied by a hematologist. Thick smears using Geimsa stain and thin smears using Wright stain were used and smear positive cases were diagnosed as malaria. The platelet counts were visually confirmed by a clinical hematologist after the counts were done by an auto analyzer machine. Platelet counts of 75,000 to 150,000/dL are defined as grade I thrombocytopenia, 50,000 to <75,000/dL as grade II and; <50,000/dL as grade III thrombocytopenia. Laboratory tests done on these patients consisted of full blood counts, liver enzymes, renal function, vitamin B12 levels, folic acid levels and erythrocyte sedimentation rate. Low folate levels were taken as < 305 nmol/L, while low Vitamin B12 levels were taken as ≤221 pmol/L⁷.

Data Analysis

Data was analyzed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA) using appropriate statistical tests.

RESULTS

Out of the total 50 cases, 31 were males while 19 were females with mean age of study population as 33.23 +/- 7.2 years. Diagnosis of P. vivax was made in 40 (80%) cases while P. falciparum was diagnosed in 10 (20%) cases. Prevalence of low folate levels was 48.0%, while the prevalence of low Vitamin B12 levels was 40%. Prevalence of low folate/ Vitamin B12 levels was 56% (Table 1). About one fourth (26%) cases had grade I thrombocytopenia while 18% and 56% had grade II and III thrombocytopenia respectively (Table 2). A significant association was observed between low folate/ Vitamin B12 levels and severity of thrombocytopenia (Table 3). No difference was observed between low folate/ Vitamin B12 levels and type of malaria (Table 4).

Table 1: Distribution of subjects based on low Vitamin B12 and Folate levels

Investigation Parameters	N (n-50)	%
Low Folate	24	48.0%
Low Vitamin B12	20	40.0%
Low Folate/ Vit. B12	28	56.0%

Table 2: Distribution of subjects based on grade of Thrombocytopenia

Thrombocytopenia	N	%
Grade I	13	26.0%
Grade II	9	18.0%
Grade III	28	56.0%
Total	50	100.0%

Table 3: Association of severity of thrombocytopenia with low vitamin B12/ folate levels

Grade of Thrombocytopenia	Low Folate/ Vit. B12		Total
	No	Yes	
Grade I	12 92.3%	1 7.7%	13 100.0%
Grade II	6 66.7%	3 33.3%	9 100.0%
Grade III	4 14.3%	24 85.7%	28 100.0%
Total	22 44.0%	28 56.0%	50 100.0%

p- value <0.01

Table 4: Association of type of malaria with low vitamin B12/ folate levels

Type of Malaria	Low Folate/ Vit. B12		Total
	No	Yes	
Vivax	17 42.5%	23 57.5%	40 100.0%
Falciparum	5 50.0%	5 50.0%	10 100.0%
Total	22 44.0%	28 56.0%	50 100.0%

p- value - 0.73

DISCUSSION

The goals of this study were to examine the association of thrombocytopenia with vitamin B12 and folic acid levels in cases of acute malaria and also to see if any difference existed between cases of falciparum and vivax malaria. We observed a significant association between low folate/ Vitamin B12 levels and severity of thrombocytopenia. Out of the total 50 cases, severe thrombocytopenia (platelets < 50,000/ dl) was observed in 56% cases while the prevalence of low folate and low vitamin B12 levels was 48% and 40% respectively. Out of 28 cases with severe thrombocytopenia, vitamin B12/ folate deficiency was observed in 24 (85.7%) cases while only 1 (7.7%) out of 7 cases of mild thrombocytopenia had low vitamin B12/ folate levels. No previous studies have investigated the role of Vitamin B12/ folate in thrombocytopenia in cases of acute malaria. Leikin S *et al.*⁶ conducted a study to evaluate the role of Folate and Vitamin B12 in the etiology of the thrombocytopenia of iron deficiency anemia. Their findings indicated that folate or vitamin B₁₂ deficiency at the bone marrow level may be involved in the causation of the thrombocytopenia of iron deficiency anemia. In another study Mant MJ *et al.*⁸, investigated the role of acute folic acid deficiency with relation to severe thrombocytopenia. Their study observes a significant association of severity of thrombocytopenia with folate deficiency. All these studies including ours, are cross-sectional in nature, thus we can only prove association between vitamin B12/ folate deficiency and

thrombocytopenia. No temporal association can be established as prospective cohort studies are required for the same. This can be taken as the limitation of the study along with its relatively small sample size. In present study, we observed no association between Vitamin B12/ folic acid deficiency with type of malaria ($p>0.05$). Out of the 40 cases of vivax malaria, low vitamin B12/ folic acid levels were observed in 23 cases (57.5%) while lower levels were observed in 5 (50%) out of 10 cases of falciparum malaria.

CONCLUSION

Vitamin B12 and folic acid deficiency is positively associated with isolated thrombocytopenia in cases of acute malaria. Thus Vitamin B12 and folic acid supplementation might help in obviating the severity of malaria and should be given in all cases of acute malaria. The results of present study should be interpreted in light of its small sample size and uni-centric nature. We thus recommend further multi-centric studies with larger sample size to validate our findings.

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