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Research Article

Changes in hematological manifestations in children with vivax malaria

Ankit Mangla, Atul Goel, Tejinder Singh*

Department of Pediatrics, Christian Medical College & Hospital, Ludhiana-141008, Punjab, India

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***Correspondence:**
Dr. Tejinder Singh,
E-mail: cmcl.faimer@gmail.com

ABSTRACT

Background: Malaria, especially Plasmodium falciparum is commonly associated with haematological abnormalities like anemia and thrombocytopenia. Vivax malaria, on the other hand was usually considered as a relatively benign illness. However over last decade or two, it is being increasingly realized that the vivax malaria is not a benign illness anymore. There have been number of reports and case series demonstrating severe haematological and clinical manifestations associated with vivax malaria mono-infection.
Methods: The study group consisted of 132 cases of vivax mono-infection diagnosed on thick and thin blood smear examination, which were recorded from the retrospective data starting from June 2002 to December 2011 and the prospective part of study from January 2012 to July 2013.
Results: Thrombocytopenia was the most common haematological manifestation in vivax malaria and has seen a significant increase from 62.9% to 87.2% from time period A to C. The proportion of children with anaemia in vivax malaria has increased from 69.4% in time period A to 78.6%. The incidence of leucocytopenia was seen in 25% cases of vivax monoinfection, with no significant change being observed over different time periods when compared among cases of vivax malaria.
Conclusions: Vivax malaria was observed to be increasingly associated with thrombocytopenia and anemia over last decade.

Keywords: Malaria, Vivax, Thrombocytopenia, Anaemia

INTRODUCTION

Vivax malaria has long been considered to have a benign course with frequent relapses. However the recent evidence from all over the world suggests that Plasmodium vivax malaria is clinically less benign than has been commonly believed.[1]

Numerous reports of thrombocytopenia, anaemia, other haematological manifestations, cerebral malaria, shock, ARDS due to P. vivax mono-infections. With this observation, we planned a study to see if there is an increase in haematological abnormalities in vivax malaria over recent decade.

METHODS

The study was conducted in the department of paediatrics at Christian medical college & hospital, Ludhiana. It included a total of 133 children from both retrospective and prospective analysis of children ≤16 years who presented to our hospital with the primary diagnosis of vivax malaria. Only slide positive cases were included in the study. The Retrospective data was collected from May 2001 to December 2011 from the hospital records. The prospective part of study involved evaluation, investigation, treatment and following up of children with vivax malaria who came to our hospital between January 2012 to July 2013.

For the purpose of comparison of the data, it was divided into 3 time periods

1. Time period A: May 2001 - June 2006
2. Time period B: July 2006 - June 2010
3. Time period C: July 2010 - July 2013

A descriptive statistical analyses and comparison was done according to 3 different time periods to evaluate the changing trend of the haematological manifestations over the period of 12 years.

RESULTS

In the study, thrombocytopenia was the most common haematological manifestation of vivax monoinfection in children. There was no difference in the rate of thrombocytopenia among different age groups. No significant difference in Platelet counts were observed between male and female patients. Thrombocytopenia was seen in 80% of the patients with vivax monoinfection with severe thrombocytopenia accounting for 16.6% cases (platelet count <20000/µL). When these cases of vivax malaria were compared with respect to 3 time periods the incidence of thrombocytopenia has increased from 63% in time period A to 85% and 87% in time period B and C respectively. It was also observed that there was a significant increase in the incidence of severe thrombocytopenia (platelet count <20000/µL). The cases with severe thrombocytopenia have increased from a mere 2.9% in time period A to 18.5% and 22.9% in time period B and C respectively (Table 1).

Table 1: Distribution of patients according to severity of thrombocytopenia.

Platelets	Time Periods		
	A	B	C
50000-149000	17 (48.6%)	7 (25.9%)	21 (30%)
20000-49000	4 (11.4%)	11 (40.7%)	24 (34.3%)
<20000	1 (2.9%)	5 (18.5%)	16 (22.9%)

In the present study despite high incidence of thrombocytopenia, the bleeding manifestations were seen in only 13.6% of cases with vivax malaria most of which were associated with clinical bleed in the form of epistaxis and GI hemorrhage (malena or hematemesis). When the patients with vivax malaria were compared among 3 different time periods, bleeding manifestations were seen in 5.7%, 25.9% and 12.9% of the patients in the time period A,B and C respectively representing an increased incidence during time period B and C as compared to time period A.

Anaemia was the second most common haematological abnormality observed in the present study. Anaemia (Hb <11 g/dl) increased from 69.4% in time period A to 74.1% and 78.6% in time period B and C respectively. Proportion of cases with mild to moderate anaemia (Hb 5-11 g/dl) has been on rise from 58.3% in time period A to 74.1% and 74.3% in time period B and C respectively. Only few cases of severe anaemia (Hb <5 g/dl) were observed in our study with no statistical significance (Table 2).

Table 2: Distribution of patients according to severity of anaemia.

Category Hb	Time period		
	A (n=36)	B (n=27)	C (n=70)
>11	11 (30.6%)	7 (25.9%)	15 (21.4%)
5-11 (mild to moderate)	21 (58.3%)	20 (74.1%)	52 (74.3%)
<5 (severe)	4 (11.1%)	0 (0.0%)	3 (4.3%)

Leukopenia (TLC <4000/µL) was observed in 22.9%, 37% and 21.5% of vivax malaria cases in time period A, B and C respectively with no statistically significant change among the 3 time periods. Though less frequent but pancytopenia was also seen in children with vivax malaria accounting for 17.1%, 19.6% and 17.1% in time period A, B and C respectively.

DISCUSSION

Thrombocytopenia is one of the common complication associated with malaria. In the present study the thrombocytopenia was present in 80% of the children with vivax malaria, with severe thrombocytopenia accounting for 16.6% cases. It is in contradiction to past studies which reported hrombocytopenia to be associated commonly with falciparum malaria and uncommonly with vivax.[2-4] Horstmann's series (1981) documented 72% of vivax cases having thrombocytopenia but none had severe thrombocytopenia.[5] But in last decade number of studies have reported severe thrombocytopenia and bleeding manifestations with vivax monoinfection.[3,6-8]

In our study when these cases of vivax malaria were compared with respect to 3 time periods the incidence of thrombocytopenia has increased from 63% in time period A to 87% in time period C, moreover rather than the incidence it's the severity of thrombocytopenia which has been of much concern and is associated with significant morbidity. In present study we have observed a significant increase in the incidence of severe thrombocytopenia (platelet count <20000/µL) from 2.9% in time period A to 18.5% and 22.9% in time period B and C respectively.

Similar observations have been seen in many studies, Makkar et al. (2002) in a study from India reported vivax malaria with severe thrombocytopenia.[9] In another study from Mumbai, in 2011 reported 68% cases with thrombocytopenia.[10] Similar study from Brazil observed

an incidence of thrombocytopenia in 58% patients with severe thrombocytopenia seen in 21 cases.[11]

In the present study bleeding manifestations were seen in 13.6% of cases with vivax malaria most of which were associated with clinical bleed in the form of epistaxis and GI hemorrhage (malena or hematemesis). When the patients with vivax malaria were compared among 3 different time periods, bleeding manifestations were seen in 5.7%, 25.9% and 12.9% of the patients in the time period A,B and C respectively representing an increased incidence during time period B and C as compared to time period A. However, only mild bleeding was usually associated with this haematological complication even for severe thrombocytopenia. A study from Karachi reported 90% incidence of thrombocytopenia with only 5% having bleeding manifestations.[12] In fact, we could not find any case in the available literature in which isolated severe thrombocytopenia resulted in death. The mechanism of thrombocytopenia in malaria is not clearly known, Fajardo in 1974 demonstrated P. vivax parasite within platelets by electron microscopy and suggested a direct lytic effect of the parasite on the platelets.[13] Recent studies have shown that the presence of thrombocytopenia in P. vivax has been associated with both non-immunological as well as immune mediated destruction, with the immune mediated destruction including the specific IgG antibody mediated destruction of platelets.[14] Oxidative stress damage of thrombocytes has also been implicated in the etiopathogenesis based on the finding of low levels of platelet superoxide-dismutase and glutathione peroxidase activity and high platelet lipid peroxidation levels in malaria patients.[15]

Anaemia in malaria is commonly associated with both vivax and falciparum malaria. The impact of vivax on haemoglobin varies from negligible to remarkable.[6,16]

In present study anaemia (Hb <11 g/dl) was seen in 75% of the vivax malaria cases and slight increase in incidence over three time periods A, B and C respectively However only 5.3% of the total vivax malaria cases presented with severe anaemia (Hb <5 g/dl). This was in keeping with the findings in other studies from India and Pakistan.[10,17] A study from Amazon region also reported 83% of patients having anaemia, but our observation was definitely less than the findings in studies from Bikaner where severe anaemia was observed in 47% cases.[9] Studies from Sudan and Brazil also observed severe anaemia in 30% cases.[18]

Haematological morbidity associated with P. vivax infection is greatest in young children especially in the tropical countries where the factors like Recurrent infections due to treatment failure and relapse, gastrointestinal helminth infection and malnutrition may have a complex interaction.[3,19,20] Parasite sequestration is not thought to be a significant cause of severe anaemia in vivax malaria. Inspite of low parasitemia compared to P. falciparum, P. vivax has a greater removal of uninfected red cells from the circulation thus leading to similar risk of severe anaemia.[20,21] An immunological response to vivax antigen higher than falciparum is also responsible for the severe anaemia in vivax malaria.[22] In our study the percentage of children with severe anaemia was more in children younger than 5 years (8%) compared to those older than 5 years (4%), this similar finding have been observed in studies from India and Indonesia.[6,16]

The incidence of Pancytopenia in our study was definitely higher in contrast to various studies from Odisha in 2002 and Amritsar in 2010 which reported pancytopenia in 0.9% and 0% of the vivax malaria cases while it is much lower than the incidence seen in a study from Uttarakhand in 2013 which reported pancytopenia in >50% cases of both falciparum malaria and vivax malaria.[23]

CONCLUSION

Thrombocytopenia is a common complication seen in vivax malaria and is no longer a distinguishing feature between vivax and falciparum. The clinicians should be aware of this change and give as much attention to vivax malaria so that they can identify the early signs of complications and severe disease. This will help in reducing the morbidity and mortality in children with malaria.

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