Original Article

Complete blood count abnormalities associated with and its response to treatment in children

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Objectives: To evaluate the hematological derangements associated with malaria and response to treatment in children.

Methodology: It was a retrospective cross-sectional study using convenience sampling, carried out in the Pediatrics and Pathology departments, Madina Teaching Hospital, Faisalabad, Pakistan from November 2012 to October 2013. All children up to age 16 years, who were suffering from malaria, were included in the study.

Results: Out of 104 children, 66 (63.5%) were male and 38 (36.5%) were female. Anemia was found in 58 (55.8%) children. Clinically, Splenomegaly was present in 75 (72.1%) of patients (p=0.04). Thrombocytopenia (platelets count <150,000/µL) was found in 82 (78.8%) of children (p=0.001). Most of the patient (91.5%) responded to 4 doses of chloroquine (CQ) and only 8.5% were CQ resistant.

Conclusion: In an acute febrile illness with marked thrombocytopenia, P. vivax malaria should be kept as a differential diagnosis. (Rawal Med J 2014;39: 261-264).

Key words: Malaria, splenomegaly, anemia, thrombocytopenia.

INTRODUCTION

Plasmodium infections are still a major health problem, resulting in millions of deaths annually worldwide.[1] Out of the estimated 3 billion people, about100 million people are at-risk to acquire vivax malaria every year.[2,3] Previously, Plasmodium falciparum was considered to be responsible for the majority of the cases with severe complications and malaria-associated mortality.[4] Plasmodium vivax malaria has now emerged as a potentially lethal condition despite of having previously been considered a benign disease.[5,6] Malaria is a true hematological infectious disease and affects almost all blood components. Anemia and thrombocytopenia are the most frequent malaria-associated hematological complications.[7] It is further complicated by the coexistence of thalassemia syndrome and other haemoglobinopathies.[8] The speculated mechanisms leading to thrombocytopenia are splenomegaly, bone marrow alterations, coagulation disturbances, antibody-mediated platelet destruction and the role of platelets as cofactors in triggering severe malaria.[9,10]

Chloroquine (CQ) plus Primaquine (PQ) is the standard treatment for vivax malaria worldwide. The initial cases of CQ resistant were reported in 1989 from Papua New Guinea followed by reports from several vivax malaria endemic countries. However, no Chloroquine resistance has been reported from Pakistan until now. Sulphadoxine-pyrimethamine (SP) in combination with artesunate have become the drug of choice against vivax malaria, which is also a recommended first line therapy for uncomplicated P. Falciparum in Pakistan.[11] Aim of this study was to find other causative plasmodium species leading to malaria in our setup, its clinical and hematological manifestations and response to treatment.

METHODOLOGY

It was a retrospective cross-sectional study using convenience sampling, carried out in Departments of Pediatrics and Pathology, Madina Teaching Hospital, Faisalabad, Pakistan from November 2012 to October 2013. All children up to age 16 years, who were suffering from malaria, were included in the study. The following data on patients were retrieved through the hospital's electronic and file records: age, gender, anemia, any evidence of bleed, splenomegaly, infecting *Plasmodium* species, malaria diagnosis methods, co-existing

conditions, results of complete blood counts (CBC), hospital course, treatment given, clinical response to treatment and improvement in platelet count after 24 hrs of completion of treatment. Laboratory records showed that Giemsa-stained peripheral blood smears (thick & thin films) were used for malaria diagnosis.

Anemia was labeled as clinical pallor along with Hb <11 Gm/dl. Thrombocytopenia was taken as platelets count <150,000/µL. Severe thrombocytopenia was labeled as platelet count <20,000/µL. Leukopenia was labeled if patient had total leukocyte count (TLC) <4000/µL. Pancytopenia was labeled in only those patients, who had suppression of all three cell lines. All data were analyzed using SPSS version 20. Chi square test of significance was applied; P<0.05 was taken as significant.

RESULTS

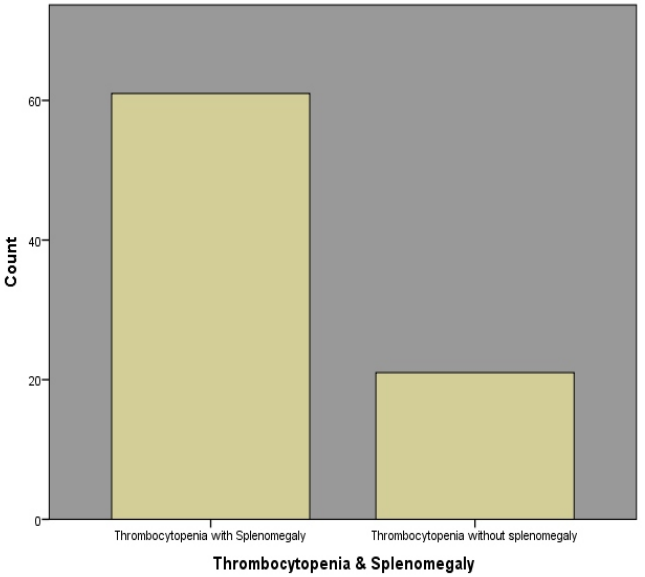
Out of 104 children included in the study, 66 (63.5%) were male and 38 (36.5%) were female. Mean age was 9.83±4.19 years (range 1-16). Mean duration of hospital stay was 3.9±1.2 days. 102 patients (98%) were suffering from Plasmodium vivax malaria. One child had Plasmodium Ovale and P. Falciparum was found in another child. The child, having Plasmodium Ovale, presented with skin bleed and epistaxis. He was found to be a case of Idiopathic thrombocytopenic purpara on bone marrow biopsy because even after completion of treatment his thrombocytopenia did not improve.

Table 1. Hematalogical abnormalities in malaria (n=104).

Abnormalities	Number	Percentage
Thrombocytopenia	82	78.8%
Anemia	58	55.8%
Leukopenia	13	12.5%
Anemia & Thrombocytopenia	44	42.3%
Pancytopenia	7	6.7%

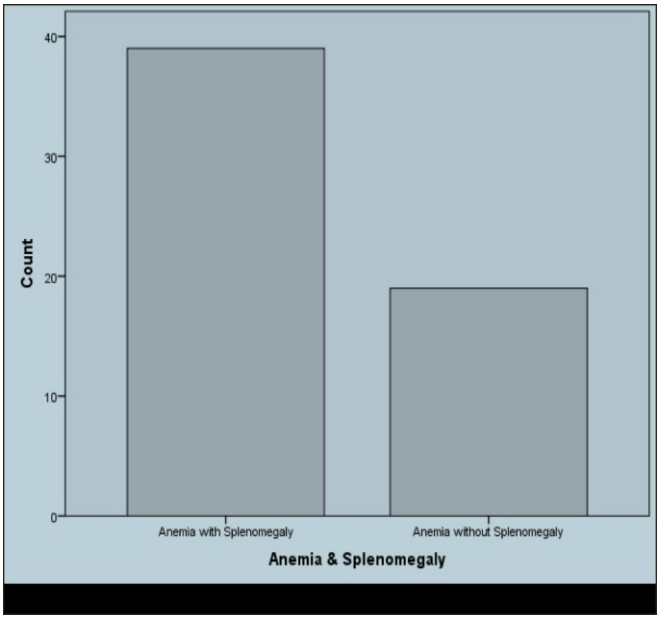
Clinically, splenomegaly was present in 75 (72.1%) of patients (p=0.04). Anemia was found in 58 (55.8%) of the children, whereas thrombocytopenia was found in 82 (78.8%) of children (p=0.001) (Fig. 1). Severe thrombocytopenia was found in only 4 (3.84%) of children. Leukopenia was present in 12.5% patients (Table 1).

Fig. 1. Thrombocytopenia and splenomegaly.



Mean Hb was 10.34±2.07Gm/dl, TLC was 6.87±2.86/µL, and Platelets were 111.83±65.35/µL. After completion of treatment, repeat mean platelets count was 146.13±68.58/µL. The relation of splenomegaly and anemia is shown in Fig. 2.

Fig. 2. Anemia and splenomegaly.



Most patient (91.5%) responded to 4 doses of CQ and only 8.5% were CQ resistant and they were treated with artimisinin based combination regimen. Out of 104 patients, 94 (89.4%) were diagnosed as a new case of malaria. Ten children (10.6%) presented with relapse (p =0.0001) because they did not take PQ for radical cure.

DISCUSSION

It is now being increasingly recognized that the vivax malaria can produce serious manifestations just like Falciparum malaria. More commonly, significant changes in hematological parameters occur even during the initial phase of clinical infection.[12] In our study, we found that 98% patients were suffering from vivax malaria. Mixed infection was not documented in any case. A study from Karachi showed that 83.1%, 13.2%, 3.7% patients had *P.* Vivax infection, *P.* falciparum infection, and mixed infections (P. vivax and P. falciparum), respectively.[13] A study from Ghandinagar, India reported that thrombocytopenia was present in 73.92% of the children suffering from malaria.[14]

In our study, platelet count less than 20000 cell/mm^3 was observed in only 2.17% patients. Thrombocytopenia was noted in 78.8% of children and mean platelets were 111.83±65.35/µL. Severe thrombocytopenia was present in 3.84% of children. Hemoglobin level was 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.[14] In our study, anemia was found in 58 (55.8%) of the children and mean Hb was 10.34±2.07Gm/dl. A study carried from Azad Kashmir on adult male patients showed that splenomegaly was present in 32.2% of cases only, whereas it was present in 72.1% of cases in our study.[15] In that study anemia was seen in 33(22.15%), neutropenia in 35(23.49%) and thrombocytopenia in 135(90.60%) patients. However, our study showed that anemia was present in 55.8%, leukopenia in 12.5% and thrombocytopenia was present in 78.8% of children. Different age group of the study population may explain this variation. Several studies have been published which showed association of thrombocytopenia with P. vivax malaria. Thrombocytopenia was seen in 93.3% in a study from Karachi[16] Similarly, and 89% in another study.[17] Thrombocytopenia was seen in 86% of patients in a study from Qatar.[18]

Leukopenia was seen in 15.2% patients in an Indian study and in 14% in a study from Dubai.[19,20] These results are very much similar to our study which showed leukopenia in 12.5% of children. The frequency of anemia seen in our patients is not comparable to other studies done in Pakistan. Two studies from Quetta, a hub for vivax malaria, found thrombocytopenia in hospitalized vivax malaria but anemia was found in only 25% and 29.5% of patients.[21,22] In our study, anemia was present in 55.8% of children. This difference in hemoglobin level may be associated with other causes of anemia, as iron deficiency anemia is very common in pediatric age group.

We also looked for response to treatment in all those patients. Most of the patient (91.5%) responded to 4 doses of CQ and only 8.5% were CQ resistant and they were treated with Artimisinin based combination regimen. In Brazil, it was found that P. vivax CQ resistance was confirmed in 10.1% of persons[23] and in vitro resistance was found to be 10.7%.[24] In our opinion, not much research work has been done in Pakistan on CQ resistance. Furthermore malaria is being misdiagnosed and we are lacking about its rational treatment. Non availability of Primaquine for its radical cure is also a risk factor for increased resistance. Out of 104 patients, 94 (89.4%) were diagnosed as a new case of malaria, whereas 10 (10.6%) presented with relapse (p=0.00001) within the study period, because they did not take Primaquine for radical cure. Thus, non availability of Primaquine may be the reason of huge burden of malaria and its resistance in Pakistan.

CONCLUSION

P. Vivax infection frequently produced abnormalities in blood counts, thrombocytopenia being the most common. Any patient presenting with febrile illness along with thrombocytopenia should be looked for malaria. Most of the patients responded to the traditional drugs. More studies are required to look for CQ resistance in various parts of

the country. The health department should take effective measures to ensure the availability of Primaquine to achieve the radical cure.

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Conflict of Interest: None declared
Rec. Date: Feb 27, 2014 Accept Date: Jun 28, 2014

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