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Research article

A study of thrombocytopenia in hospitalized vivax malaria patients

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ABSTRACT

Objective: To assess the occurrence and severity of thrombocytopenia in hospitalized vivax malaria patients.

Design and setting: Retrospective and descriptive hospital based case series from March 2005 to March 2007, conducted in the medical unit of Al Khor Hospital.

Patients and methods: Seventy-eight patients with peripheral smear positive were enrolled in the study. Peripheral smear examination for malaria parasites was used as the method of choice for the diagnosis of malaria. Hematological parameters were determined by using an automated analyzer. Low platelet counts were re-evaluated by manual methods.

Results: Study sample was 78 patients, of which 65 patients (83.3%) were thrombocytopenic. Of these, 41 patients (52.6%) had mild thrombocytopenia, 23 patients (29.5%) had moderate thrombocytopenia and 1 patient (1.3%) had severe thrombocytopenia. All patients (100%) were male.

Conclusion: High prevalence of thrombocytopenia was seen in vivax malaria patients, making it a common hematological feature in vivax malaria.

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INTRODUCTION

Malaria affects approximately 5% of the world population, is transmitted through 103 countries and causes 1–3 million deaths each year. About 270 million people are infected each year. Malaria is multisystem infection, but the effects on renal, haematological and central nervous systems increase the mortality rate.¹ With the emergence of advanced laboratory and investigational aids, it has now become fairly clear that the malaria parasite produces haematological dysfunction.²

Malarial hematopathy attempts to describe the involvement of one or more hematopoietic cell lines and includes the endothelial dysfunction that can give rise to the thrombotic microangiopathy that may evolve into a consumptive coagulopathy. Platelet abnormalities are both qualitative as well as quantitative. Thrombocytopenia is a common occurrence in acute malaria. It is attributed amongst other factors to excessive splenic platelet pooling and a shortened platelet life span.

Thrombocytopenia appears to be associated with elevated serum concentration of both pro and anti-inflammatory cytokines, although their exact role is still under investigation. Protein aggregates, red cell and white cell fragments are known to interfere with platelet counts in automated blood analyzers, giving rise to erroneous normal platelet counts.³ Thrombocytopenia has been identified as a key indicator for malaria in patients with acute febrile illnesses. Thrombocytopenia occurs in both infections due to *Plasmodium vivax* as well as *falciparum*. It also must be remembered that very low platelet counts can be encountered in both *vivax* and *falciparum* malaria and that they may not necessarily have prognostic implications or merit platelet transfusions.^{4,5} Clinical bleeding in malaria due to thrombocytopenia is not common even with very low platelet counts, unless a co-existing coagulopathy is present.⁶

We conducted this study to assess the occurrence and severity of thrombocytopenia in hospitalized patients with *vivax* malaria.

PATIENTS AND METHODS

This study was retrospective and descriptive between the period of March 2005 to March 2007 on all adult malaria patients admitted to the medical unit at Al Khor Hospital in Qatar. A total of 78 patients were enrolled. Malaria patients who were only seen and discharged in the A&E department and those who attended as out patients were excluded from the study.

Data was collected by utilizing patient medical records, details of history and clinical assessment and a pre-tested questionnaire. A standardized data collection form was used to extract data from patient records. Laboratory diagnosis of malaria was based on thin blood film using Wright's stain and thick film using Giemsa stain. The platelet count was performed using Coulter LH 750 apparatus, after collecting samples taken in EDTA tubes.

Reduced platelet counts were re-evaluated by a manual method. Patients with thrombocytopenia were divided into three categories;

- (1) Mild Thrombocytopenia < 150,000 to > 50,000/L
- (2) Moderate Thrombocytopenia < 50,000 to > 20,000/L
- (3) Severe Thrombocytopenia < 20,000/L

Drugs used in the treatment were:

Quinine Phosphate: 600 mg Q 8 hr (I.V, Oral) for 7 Days

Chloroquine Phosphate: 250 mg 4 tab initially then 2 tab after 6 hours and then 2 tab daily for two days

Primaquine Phosphate: 15 mg orally once daily for 15 days

Doxycycline: 200 mg orally daily for one week

Data was entered into the computer from master tables and data analysis tool packs and simple percentage analysis performed utilizing MS-Windows applications specifically MS-Access & MS-Excel.

The study protocol was reviewed and approved by the ethical committee (Hamad Medical Corp. – Medical Research Centre).

RESULTS

A total of 78 patients with malaria were enrolled in the study. Sixty five (83.3%) patients had thrombocytopenia.

In vivax malaria, 49 patients had thrombocytopenia (86%) and this was further distributed in to mild in 29 patients (50.9%), moderate in 19 patients (33.3%) and severe in one patient (1.8%). In the falciparum group six patients (85.7%) had thrombocytopenia.

In the mixed group 9 patients (75.0%) had thrombocytopenia, while in the ovale group 1 patient (50%) had thrombocytopenia.

By age, the 78 all-male sample were expatriate workers with 60% in their 20's (n = 47), 30% in their 30's (n = 23) and the remaining 8 patients (10%) belonging to ages above 40 years.

By nationality, 57 patients (73%) were Indians, 10 patients (13%) were Pakistanis, while the rest of 11 patients represented various other nationalities.

Comorbid conditions, such as diabetes mellitus, coronary artery disease and hypertension, were seen in one patient (1.3%).

None of these patients required platelet transfusion and in 51 patients (78.5%) of the thrombocytopenic group, platelet counts had recovered completely prior to discharge. However, 14 patients (21.5%) remained thrombocytopenic at the time of discharge and were lost during follow up.

Seventy-seven patients (98.7%) presented with fever, chills and sweating. Nausea and vomiting were seen in 36 patients (46.3%), whereas headache presented in 33.3% of patients. Duration of symptoms lasted from a minimum of one day to a maximum of 15 days.

Splenomegaly was found in 20 patients (25.6%)

Fever was documented in 82% patients

Fifteen percent of patients had hypotension

Thirteen percent of patients had jaundice, whereas anemia was encountered in 11.5% of patients.

History of travel to endemic countries (Origin) was reported in all (100%) of the 78 patients.

Complications including jaundice and anemia were seen in 10 patients (12.8%)

All patients (78) were cured.

Forty-seven patients (60.2%) had previous history of malaria while 31 patients (39.7%) were fresh cases. None of the patients had hemorrhagic manifestations.

DISCUSSION

Thrombocytopenia is also seen in patients with acute febrile illness due to viral causes, but its presence is considered as important diagnostic clue for malaria in endemic areas - as suggested by previous investigators⁷ and particularly so when associated with anemia.⁸

Interestingly all 78 patients were males and of this group, Indians are the most predominant nationality with 57 patients (73.1%) compared to other nationalities and this is possibly explained by the high number of Indian expatriates in Qatar in comparison to other nationalities.

The high prevalence of malaria seen in the young working group of 70 patients (90%) could be attributed to the fact that most of the expatriate workers are young individuals. In older groups, all 8 patients (100%) had thrombocytopenia, possibly reflecting that older people are more prone to thrombocytopenia when exposed to malaria parasites. Most malaria patients presenting at our hospital were infected with *Plasmodium vivax*, with other species rarely encountered.

In this study we focused on *Plasmodium vivax* as the other species were too small to be studied. Of the 57 patients with vivax malaria, thrombocytopenia was encountered in 49 patients (86%) and that was divided further to mild 29 patients (50.9%), moderate 19 patients (33.3%) and severe 1 patient (1.8%).

These findings are higher than those reported by other investigators, 70% by Abdul Rauf Memon⁹ 71% by Robinson¹⁰ and 59% by Rodriguez et al.¹¹ Bashwari et al from Saudi Arabia reported anemia in 60% and Thrombocytopenia in 53% of cases.¹²

Comorbid conditions seen in the study included diabetics mellitus, hypertension and coronary artery disease, and were all seen in one Sudanese patient with age above 50 years. This reflects that the majority of the patients were young, healthy people (Table 1).

Chills and sweating were found to be the most common presenting symptoms, seen in 77 patients (98.7%) and this finding conforms with the previous studies.

Splenomegaly was seen in 20 patients (25.6%), being the commonest sign after fever and can be attributed to many mechanisms. Interestingly all 78 patients (100%) reported a history of travel to their home countries where they have contracted the disease, and this indicates that Qatar is not an endemic country for malaria, as no local citizens were found to have malaria.

Table 1. Demographic data.

	Age Group	Number of Patients	Percentage
Age (Years)	20–30	47	60.2%
	31–40	23	29.5%
	41–50	7	9.0%
	51–60	1	1.3%
Gender	Male	78	100%
	Female	0	0%
Nationality	Philipino	1	1.3%
	Indian	57	73.1%
	Sri Lankan	1	1.3%
	Pakistani	10	12.8%
	Nepalese	8	10.2%
	Sudanese	1	1.3%
Comorbid Conditions	DM	1	1.3%
	HTN	1	1.3%
	CAD	1	1.3%
	Respiratory Disease	0	0.00%
	Renal Disease	0	0.00%
	Others	0	0.00%

Key: DM, Diabetes Mellitus; HTN, Hypertension; CAD, Coronary Artery Disease.

High prevalence of relapse was encountered in these patients (47 patients- 60.2%) and this is not surprising in vivax malaria. The clinical importance of this is that all our vivax patients received primaquine 15 mg orally, daily, for two weeks, provided they had normal G6PD levels, to prevent future relapse.

Of the vivax and mixed groups, 60 patients (76.9%) received chloroquine 250 mg, four tablets initially, then two tablets after 6 hours and two tablets daily for 3 days, followed by primaquine. The response to antimalarial therapy was excellent. Patients were cured and discharged in good condition and the platelet counts recovered in 51 patients (78.5%) of the thrombocytopenic group prior to discharge. However, in 14 patients (21.5%) the platelet counts remained low at discharge, but we cannot conclude that there was failure of response as these patients were lost during follow-up.

Despite the high prevalence of thrombocytopenia, none of our patients required platelet transfusion or had hemorrhagic manifestations, indicating that low platelet counts may not necessarily have prognostic implications and only represent transient phenomenon.

CONCLUSION

High prevalence rate of thrombocytopenia in patients with vivax malaria was observed in our study, however, this may only represent transient phenomenon and is probably of no significant prognostic value. Quick recovery after treatment was the rule, without requirement for platelet transfusion. In light of the observation made in our study, even though thrombocytopenia is pronounced in vivax malaria, patients can be safely treated and discharged from emergency rooms without hospital admission. This, in turn, makes treatment of such patients cost-effective without compromising their recovery.

Thrombocytopenia is a key indicator for malaria in patients with acute febrile illness coming from endemic malaria areas.

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