MEDICAL CHANNEL

Original Article

PLASMODIUM VIVAX BENIGN TERTIAN FEVER: NOT ANY MORE !

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Received on: 01-05-2016
Accepted on: 21-08-2016

ABSTRACT

Background: To document the recent growing health problem and burden due to malignant behavior of the most common malarial subtype Plasmodium Vivax, which is traditionally known for its benign nature.**Objectives:** Plasmodium vivax malaria is considered a benign form of malaria, however, In Pakistan it has undergone complete metamorphosis and present features that deny them to be considered as benign. The objective of the study is to verify that Plasmodium vivax malaria in Pakistan is a malignant and no more benign.**Methods:** A retrospective study of patients admitted to Medical Unit.I, JPMC, Karachi was done who were positive for plasmodium vivax (PV) or plasmodium falciparum (PF) or both. All had severe malaria. **Results:** A total of 330 patients were included. These included patients who were positive for PF or PV or both. Out of 330, 110 (33.3%) were positive for P.Falciparum, 208 (63.03%) were positive for PV and 12 (3.63%) were positive for both PV and PF. Virulence of PV is shown by fact that thrombocytopenia, anaemia and renal failure were seen in 88 (42.12%), 46 (22.12%) and 67 (32.21%) patients respectively. In PV patients mortality rate was 3.8% out of 210 patients died. These findings are unusual for PV which is historically known for its benign nature. **Conclusion:** Recognition of malignant behavior of p vivax is very important in dealing with complicated malaria. Thromobcytopenia is seen in almost every patient with malaria. It is more of a diagnostic rather than prognostic factor.

Key Words: Malignant, Behavior, Thrombocytopenia, Malaria

Med. Channel 2016; 22(3) 30-34

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INTRODUCTION

Malaria is still rampant throughout the world especially in tropical areas, causing a high number of deaths especially in children. It remains a major cause of global mortality[1]. Increasing ease of rapid worldwide travel has raised concerns about its swift spread around the globe. A resurgence of dormant plasmodium vivax was recently seen in South

Korea[2] . Malaria remains common in travelers from nonendemic areas to the tropics due to increase in travel and lack of immunity such travelers [3,4,] . A lack of effective medicine for eradication of p vivax and a escalating drug resistance to primaquine are also important factors[5,6] contributing to high incidence of PV. This has led to a grim health situation. Approximately 300-500 million people are at risk. Malaria is a curable disease especially if treatment is started early. This creates a formidable challenge[7].

Severe malaria is characterized by signs of severe illness, organ dysfunction and a high parasite load (peripheral parasitemia of 5% or 200,000 parasites/ mcL). Severe malaria is associated with high mortality and morbidity, especially in the young. The young population of Pakistan is at risk [8].

Risk is also high in pregnant women and the immunocompromised . Risk has increased also due to resistance developed by female mosquitoes to insecticides. Heavy rainfall and stagnant water resulting from the irrigation system are responsible for high prevalence of malaria in Pakistan[9, 10].

Plasmodium vivax is classically known as a relapsing disease. The risk factors include male gender, young age, high gametocytemia, anemia associated plasmodium falciparum gametocytemia and resistance to primaquine. Plasmodium vivax malaria has become a major health problem but has been grossly neglected and underestimated. This is surprising especially since it is known that it is the most prevalent and most common type of malarial subtype and can have dire impact[11].

The classical presentation includes fever, chills, fatigue and sweating. Malaria represents a medical emergency which has the potential to deteriorate and its complications may be fatal. It is curable if prompt treatment is initiated. It is considered a dangerous global health problem[12, 13].

The main feature of severe malaria is sequestration of erythrocytes in major cerebral, renal, hepatic and pulmonary arteries. Patients may develop single or multiple organ failure, manifesting as cerebral malaria, renal failure, circulatory collapse, severe anemia, hemoglobinuria, abnormal bleeding, adult respiratory distress syndrome (ARDS) and/or jaundice etc[14,15,16,17,18,19].

Diagnosis is made mostly on clinical grounds but can be substantiated by finding malarial parasite on Giemsa a staining in the peripheral blood film. Single smears are usually positive in infected individuals. High parasitemias (especially 10–20% of erythrocytes infected or 200,000–500,000 parasites/mcL) or the presence of malarial pigment (a breakdown product of hemoglobin) in 5% of neutrophils are associated with a particularly poor prognosis[16].

MATERIAL AND METHODS

A large study was conducted in Medical Unit.I, Jinnah Postgraduate Medical Centre (JPMC), Karachi during February 2015 to January 2016. A total of 330 patients were included in the study. Malarial parasite was detected in the thick peripheral film blood films of all patients. Based on the cytological details of MP recorded by examination of thin films, patients were divided into 3 groups

1. Those who were positive for p.falciparum: 110 patients .
2. Those who were positive for p.vivax 208 patients.
3. Those whose blood films were positive for both p.falciparum and p.vivax : 12 patients

Exclusion Criteria are

1. Febrile thrombocytopenia of other causes.
2. Chronic Liver disease
3. Fever of other established cause

All patients were from Karachi.Every patient received standard medical treatment (for p.vivax) with primaquine (0.5mg/kg/day) for 7 days[17] (In case of P.vivax).Patients were discharged after clearance of malarial parasite(MPs) on peripheral blood films and clinical recovery.In 2006, WHO recommended that severe p.vivax malaria should be treated with injectable anti-malarial drugs[18].A detailed history was taken, followed by physical examination to assess the gravity of the situation and presence of any complications. Other investigations were also performed which included fasting blood sugar, blood urea, serum creatinine, liver function tests and x-ray chest PA view. The observational study design based on cross-sectional survey was used as the study does not interfere with the occurrence of the event (Plasmodium vivax malaria). The collected data was analyzed using SPSS Statistics version 15.0 for Windows version.

RESULTS

All 330 patients included in the study were suffering from severe and complicated malaria at the time of

TABLE NO.1

	P Falciparum	**P Vivax**	**Both P Flaciparum and P Vivax**
Number of Patients	110(33.3%)	208(63.03%)	12(3.63%)

TABLE NO.2

	P Falciparum 110	**P Vivax 208**	**Both P Flaciparum and P Vivax 12**
Thrombocytopenia	75 (68.2%)	208(100%)	11(91.7%)
Bleeding	42(38.2%	0(0.0%)	5(41.7%)
Hemoglobin	44(40.0%)	46(22.1%)	7(58.3%)
Acute Renal Failiure	68(61.8%)	65(31.3%)	9(75.0%)
ARDS	21(19.1%)	4019.2%)	2(16.7%)
Cerebral Malaria	96(87.3%)	8(3.9%)	1(8.3%)
Hypotention	68 (61.8%)	44(21.2%)	2(16.7%)
Liver Disease	17(15.5%)	5(2.4%)	1(8.3%)
Mortality	80(72.7%)	8(3.9%)	2(16.7%)

admission. Of these, 208 (63.03%) patients were positive for p.vivax on peripheral blood smear, 110 (33.3%) were positive for p.falciparum and 12 (3.63%) patients had smears positive for both (Fig.1 & Table.1). Out of 208 patients with plasmodium vivax malaria 1 18 (56.3%) were males and 90 (43.7%) were females. Similarly, out of 110 patients with plasmodium falciparum infection, 33 (30%) were female and 77 (37.01%) were male. Of the 12 patients with combined infection, 7 (58.4%) were males and 5 (41.6%) were females.

Thrombocytopenia (Pl. count <100000) was seen in all patients with plasmodium vivax malaria; in 75 out of 110 (68.10%) patients who were positive for plasmodium falciparum malaria and in 5 out 12 (41.66%) patients with mixed vivax and falciparum infection.

It generally takes 4 days to recover after treatment. None of p.vivax patients with thrombocytopenia showed signs of bleeding from any site or rashes. However, there was high incidence of bleeding and rashes in plasmodium falciparum patients, with 42 out 75 (56%) patients suffering from those symptoms. 5 out of 12 patients in the mixed variant group also developed bleeding diathesis.

The total leukocyte counts were less affected in these complicated malaria patients. .

Mortality was highest within the plasmodium falciparum group i.e. 80 out of 110 (72.7%) patients. 8 patients out of 208 (3.8%) with plasmodium vivax infection group and 2 out of 12 patients (16.7%) in the mixed group the other finding can be recognized from the Fig.2 & Table 2.

DISCUSSION

Severe malaria occurs when infection is complicated by organ failure. The treatment of severe vivax malaria has to be the same as that for severe plasmodium falciparum malaria. The manifestations of severe malaria include:

- CNS involvement with abnormal behavior, impairment of consciousness, seizures, coma or other

FIGURE NO.1

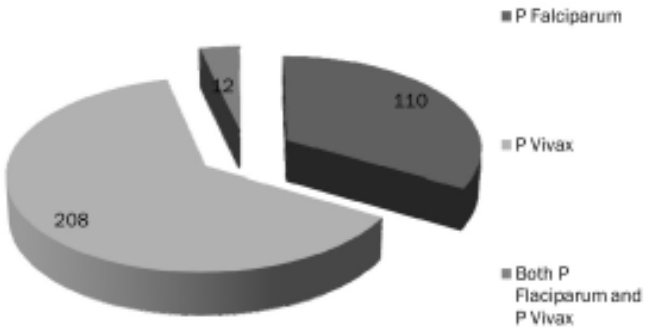
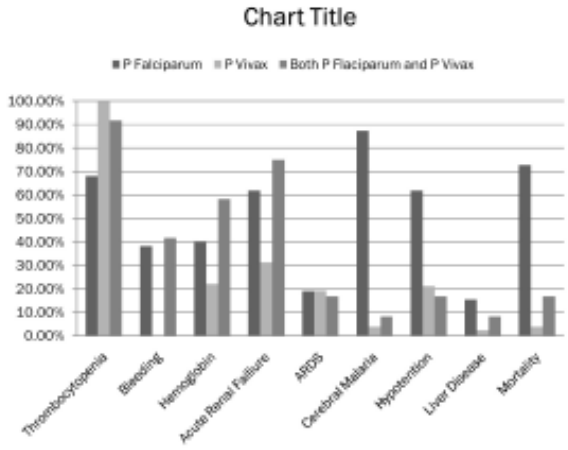


FIGURE NO.2



neurologic abnormalities[17,18].

- Hemolytic anemia, thrombocytopenia, Disseminated Intravascular coagulation (DIC) etc. Hemoglobinuria (hemoglobin in the urine) due to hemolysis[7].
- Low blood pressure caused by cardiovascular collapse.
- Acute renal failure and metabolic acidosis[14]
- Hypoglycemia may be seen in uncomplicated malaria or after treatment with quinine. It can also occur due to hyperparasitemia where the count is more than 5%.[11].

Although less virulent than plasmodium falciparum, plasmodium vivax can also cause complicated malaria and is often associated with severe disease. The frequency of severe vivax malaria is alarming especially when considering that it is the most common malaria subtype[15,10] .

It has been calculated that up to 40% of patients who have plasmodium vivax malaria develop these complications. Approximately 80% of Pakistan is at risk[11].

Thrombocytopenia is the most common complication. All patients in our study had thrombocytopenia. However, It is more of diagnostic rather than prognostic value. P.vivax malaria is often confirmed by finding a febrile patient with low platelets. It is supported by results from studies[20,21] and it is not supported by[22,23]

The affliction of liver by malarial parasites is well known.[24].

Acute respiratory distress syndrome (ARDS) was seen in 2% and 3% patients in studies[25].

Cerebral malaria with plasmodium vivax is associated with high mortality[17.18].

Significant hypotension is also a feature of complicated malaria both with plasmodium vivax and falciparum, seen especially in young patients. Severe anemia is a feature of malaria. It is a bad prognostic sign as compared to thrombocytopenia which mainly has diagnostic value.

Hypoglycemia is more common with plasmodium falciparum malaria compared to plasmodium vivax or mixed malaria[20].

CONCLUSION

It is evident that we are facing the on slaught of a new emerging, resistant form of Malaria. However, complications are milder compared to plasmodium falciparum malaria. Thrombocytopenia is the most common complication of plasmodium vivax. The present study may not only help inform the general public as well as physicians, help in facilitate local, national and international health policy and facilitate local medical decision making. Thrombocytopenia has general importance more as a diagnostic rather than a prognostic tool .

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Authors contribution:
* Researcher and writing the manuscript, ** Write up, correction, collection data *** Review the manuscript and data analysis

Conflict of interest: The authors declare no conflicts of interest.