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# CLINICAL AND HEMATOLOGICAL PATTERN IN PATIENTS WITH PLASMODIUM VIVAX

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**ABSTARCT**

**Objective:** To study the clinical and hematological pattern in patients with Plasmodium Vivax infection.

**Methods:** This multi-centre cross-sectional study was conducted from April 2010 to October 2010 simultaneously at Civil Hospital Karachi, Kulsoom Bai Valika Social Security Hospital S.I.T.E and Metro Lions Hospital Metroville Karachi. 150 patients between 5 to 14 years of age with positive malarial parasite or ICT Malaria for Plasmodium Vivax or both P Vivax and P Falciparum were included in the study. Frequencies of gender, various symptoms and signs were determined, while age and laboratory alterations (Hemoglobin, White Cell and Platelet Count) were calculated by Mean + SD.

**Result:** Most of the patients were enrolled during July to September in rainy season. 75% patients had fever of less than 2 weeks duration. Hepatosplenomegaly was detected in 49 patients. Thrombocytopenia (Platelet less than 150 x 109/L) and anemia (Hb < 10gm/dl) were found in 91% and 73% respectively. Leucopenia (less than 4 x109/l) was present in 59 (39%) and neutropenia (ANC < 1500) was found in 22 (14.7%) patients.

**Conclusion:** Clinical manifestations of plasmodium vivax infection ranged from asymptomatic to severe complications including cerebral malaria, acute renal failure, acute hemolytic crisis and hepatic dysfunction. Acute onset fever and hepatosplenmegaly were most common clinical manifestations found in 75% and 32.6% cases respectively. Anemia and thrombocytopenia were more frequent haematological parameters whereas leucopenia was less common in this study.

**Key Words:** Plasmodium Vivax, Clinical, Haematological,Parameters

## INTRODUCTION

Malaria is a disease of tropical and subtropical countries particularly Africa and Asia. Despite advances in knowledge, it continues to cause significant morbidity and mortality worldwide. It is one of the most prevalent human infections in the world, it is estimated that 300-500 million cases and 1.5-2.7 million deaths occur each year. Mortality rate is usually high (20%) in severe malaria (parasitemia >5%).[1] The burden of malaria in Asia has been under appreciated, despite recent evidence, suggesting that the continent contributes almost 40% of the global malaria cases. In Asia, P. vivax often accounts for 50% of the malaria prevalence, and yet the morbidity associated with this infection and its spectrum of disease is largely ignored .[2]Although P. vivax is widely regarded as benign, its propensity to recur is increasingly recognized by clinicians in endemic areas ,resulting in appreciable disease, particularly in young children. There have been increasing numbers of case reports describing severe manifestations of vivax malaria in recent years, however, the true incidence of severe vivax malaria is unknown. Recent studies have highlighted the association between vivax malaria and life-threatening manifestations, such as respiratory distress, severe anaemia, and neurological manifestations with coma, placing Plasmodium.

vivax infection at a higher status as a global health concern.[3] Infection with Plasmodium vivax, particularly in temperate areas of India, causes symptoms up to 6-12 months after the host leaves the endemic area. In addition, patients .infected with P. vivax or P .ovale may relapse after longer periods because of the hypnozoite stage in the liver.[4] In most of the studies fever, anemia and splenomegaly were reported in more than 80% of cases with high incidence of falciparum(65%) as compared to Vivax (35%). Gastrointestinal symptoms were more in falciparum whereas generalized bodyache, cough and hepatosplenomegaly were main features of vivax infection.[5]

Hematological changes, which are one of the most common complications, play an important role in increasing mortality. Hematological abnormalities that have been reported include anemia, thrombocytopenia, atypical lymphocytosis and rarely disseminated intravascular coagulation.[1]

Anaemia has frequently been associated with malaria. Two common causes of anaemia are increased haemolysis and decreased rate of erythrocyte production from bone marrow whereas the malnutrition and intestinal parasitic infections aggravate this problem in highly endemic areas. In a study about 50% patients with P.falciparum and mixed infections were anaemic while 29% of P.vivax infected cases had this abnormality. White cell counts were also found reduced in about 20% infected with various plasmodium species.[6]

Low platelet count is one of the life threatening complications associated with malaria. .Thrombocytopenia in vivax malaria appears to be immune mediated and occurs in the absence of blood coagulation activation. In contrast, thrombocytopenia in falciparum malaria is most often accompanied by activation of the coagulation cascade.[7]Thrombocytopenia is reported in up to 70% and severe anemia in 25% of malaria patients whereas leukocyte count may be normal or low; leukocytosis is seen in less than 5% of cases and is a poor prognostic factor. Liver function test results are often abnormal; transaminase levels are elevated in about 25% of cases, bilirubin in one-third and lactose dehydrogenase in up to 80% cases.[8]

In one of the studies from India, the proportion of patients having severe manifestations, including severe anemia, thrombocytopenia, cerebral malaria, acute respiratory distress syndrome, hepatic dysfunction, renal dysfunction, abnormal bleeding was significantly high in association with P. vivax monoinfection in 0-5 year age group, while the same was significantly high in association with P. falciparum monoinfection in 5-10 year age group[9], similar pattern is observed in local data. Government health sector provides health care to large number of patients but still a sizeable population seeks health facility from private health clinics where bulk of malaria cases are treated empirically with inadequate protocols, in addition there is lack of awareness regarding early recognition, severity of the disease and its laboratory diagnosis, as a result most of the patients end up with complications and high mortality rate.. Early recognition and management can prevent morbidity and mortality due to vivax malaria. Recent cumulative local data regarding various clinical and haematological manifestations from different areas of Karachi is still deficient therefore this multi-centre study was done to determine the clinical and hematological pattern of patients in plasmodium vivax infection.

## METHODOLOGY

It was a multi-centre cross sectional study conducted from April 2010 to October 2010 simultaneously at Civil Hospital Karachi, Kulsoom Bai Valika Social Security Hospital S.I.T.E and Metro Lions Hospital Metroville Karachi. Civil Hospital Karachi is one of the largest public sector teaching hospital and caters nearly 400 to 500 paediatric OPD patients daily from urban and peri urban areas of the city, Kulsoom Bai Valika is a semi government and Metrolions is a private Trust hospital each providing health facility to 100 to 200 children coming from Site industrial area of Karachi. Most of the patients seeking health care in these hospitals belong to middle and low socioeconomic status. A total of 150 patients between 5 to 14 years of age , who presented in OPD or admitted in ward with positive malaria parasite or ICT Malaria for Plasmodium Vivax or both P. Vivax and P. Falciparum were included in the study with non probability sampling technique. Out of 150 patients 59 were from Kulsoom Bai Valika, 50 from Metrolions and 41 were enrolled from Civil hospital Karachi. Patients with isolated P Falciparum were excluded from the study. After establishing the diagnosis, clinical evaluation was done and information regarding age, duration of fever, presence of bleeding, jaundice, hematuria or oliguria, splenomegaly and hepatomegaly was recorded. At the time of enrollment in the study, blood samples were obtained from each patient to assess complete blood count and differential leukocyte count. ICT malaria was done in febrile patients having either pancytopenia or thrombocytopenia with negative MP slide. Bilirubin, alanine aminotransferase, urea, creatinine, and blood sugar levels were done in patients with systemic involvement such as jaundice, oliguria and coma.

Data was entered in SPSS version 15. Frequencies of gender, various symptoms and signs were determined. While age and laboratory alterations (Hemoglobin, White Cell and Platelet Count) were calculated by Mean + SD.

## RESULT

During study period, 150 patients were enrolled, out of them 59(39.3%) were from Kulsoom Bai Valika Hospital, 50(33.3%) from Metro Lions Metroville Hospital and 41 (27.3%) were from Civil Hospital Karachi, Most of the patients were enrolled during July to September in rainy season. (Figure I). Among 150 patients, 93 (62%) were male and 57 (38%) were female. Their mean age was 6.73 + 3.36 years with range of 5 to 14 years; most of them (43%) were between 5 to 8 years.

Out of 150 patients, 10 showed plasmodium Vivax and Falciparum both, 129 patients showed isolated plasmodium Vivax on peripheral smear while 11 patients had positive Plasmodium Vivax by ICT malaria test. All the patients presented with fever, most of them (75%) had fever of less than 2 weeks duration only 11 % had fever for more than one month duration. Hepatosplenomegaly was detected in 49(32.6%), isolated hepatomegaly in 14(9.3%) and splenomegaly in 22(14.6%) patients. Seven out of ten patients with both P Falciparum and P Vivax had hepatosplenomegaly. Regarding severe systemic involvement one patient presented with acute renal failure, this patient had anuria for 2 days, with urea of 200 mg/d l and creatinine 3 mg/dl and was recovered after dialysis. Another patient had cerebral malaria, showing mixed infection with P Falciparum and P Vivax, and recovered after treatment. Only one patient who presented with acute hemolytic crises, hemogolbinurea and jaundice was expired. Three patients developed recurrence of Plasmodinmu Vivax after two month of treatment despite taking full treatment probably due to persistent exposure to vector.

**FIGURE 1**
**DISTRIBUTION OF PATIENTS WITH PLASMODIUM VIVAX (n=150)**

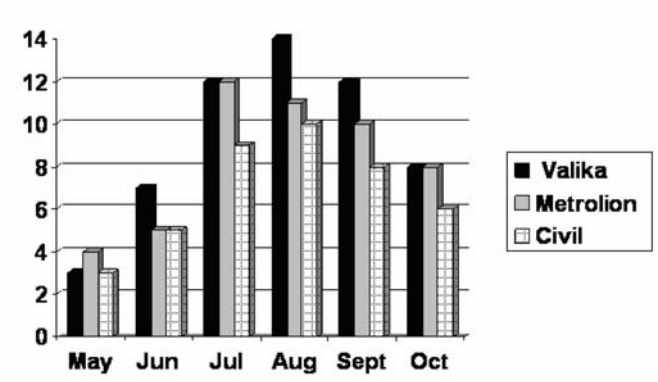



**TABLE I**
**HEMATOLOGICAL PARAMETERS OF PATIENTS WITH PLASMODIUM VIVAX**

| | MEAN + SD | RANGE |
|---|---|---|
| **HEMOGLOBIN (gm/dl)** | 8.3 + 2.46 | 2.7 - 14 |
| **WHITE CELL COUNT ( x $10^6$ / µL)** | 6573 + 3744 | 2400 - 24700 |
| **ABSOLUTE NEUTROPHIL COUNT (x $10^6$ / µL)** | 3127 + 1913 | 620 - 10200 |
| **PLATELET COUNT ( / µL)** | 83346 + 45873 | 9000 - 220000 |

Hematological parameters showed variable results. (Table.1) Thrombocytopenia (less than 150 x 109/L) was almost identical approximately in 91% patients, 73% had platelet count below one lac, out of them 27% had platelet count below 50,000. Only four patients had platelet count below 20,000 out of which two had bleeding tendencies and required platelet transfusion.

Anemia (Hb < 10gm/dl) was observed in 110(73%) patients, 18(12%) were severely anemic (Hb below 5gm/dl) and 27 (18%) had moderate anemia (Hb between 5 – 7 gm /dl). Out of 18 severely anemic patients 14 had hepatospenomegaly probably due to hemolysis. Leucopenia (less than 4 x109/l) was present in 59 (39%) whereas neutropenia (ANC < 1500) was found in 22 (14.7%) patients.

## DISCUSSION

Plasmodium vivax is responsible for wide spread clinical symptomatology ranging from asymptomatic, mild fever to severe complication like cerebral malaria.[10] It is one of the frequent presenting illnesses at the paediatric out patient department and also one of the leading causes of hospital admissions due to severe malaria.[11] Previously complicated malaria was rarely reported but recently changing clinical pattern has shown the association of emerging trends of complications with vivax malaria.

In the current study we determined the clinical and hematological findings in plasmodium vivax and mixed plasmodium vivax and falciparum infections at three health facilities catering urban periurban and slum areas of Karachi.

Most of the patients in our study were between 5 to 14 years of age with the mean age of 6.73 + 3.36 years in contrast to an earlier study which reported mean age of two years.[12] Information regarding age and gender related prevalence of malaria is scarce but most of the studies reported generally a high burden in males compared to females, [13] our study also showed similar results. In the current study majority of cases presented during rainy season of July to September, the reason could be the favourable humid climate and warm stagnant water with aquatic vegetations for mosquito vector breeding, other local studies also reported similar findings.[14]

Fever for seventy two hours or high temperature found during clinical examination is an essential feature for diagnosis of uncomplicated malaria.[15] In our study maximum number of patients (75%) came with fever of short duration whereas another study also showed increased frequency (76%) of fever in plasmodium vivax infection.[6] In the present study mixed infection with plasmodium vivax and falciparum was found in 15% of cases which is in contrast to another local study which showed 1.5% of mixed infection,[16] High incidence of mixed vivax and falciparum in our study is probably due to emerging drug resistance to these species and high endemicity of malaria infection in Karachi.

Hepatosplenomegaly was found in 32.6% of patients whereas isolated hepatomegaly was observed in 9.3% and splenomegaly was present in 14.6% cases in the present study. This data is comparable to other studies in which hepatomegaly was found in 8.2% and 4% patients respectively.[6,17] Splenomegaly on the other hand is reported to be a more frequent clinical sign and its frequency ranged from 8-13% in various international studies[17,18] whereas local data showed a relatively high proportion 20%.[19]

Thrombocytopenia is one of the major clinical presentations of severe plasmodium

Vivax malaria.[20.21] Our study showed thrombocytopenia in 91%and anemia in 73%, this is comperable to another local study which showed thrombocytopenia in 86% and severe anemia in 42% patients. [22]

Although plasmodium vivax infection is associated with mild symptomatology, proportions of severe complications are found to be quite high in children. Common

severe problems reported in various studies include cereberal malaria, acute respiratory distress syndrome, hepatic dysfunction and multiorgan dysfunction (MOD).[9] In the current study severe manifestations were less frequent, acute renal failure, cerebral malaria and acute haemolytic crisis with hepatic dysfunction were observed in one patient each, cerebral malaria was found in mixed falciparum and vivax infection and responded to treatment while patient with acute haemolytic crisis was associated with plasmodium vivax monoinfection and expired eventually. Three patients relapsed even after adequate treatment according to WHO guidelines. These observations reflect the menace of emerging drug resistance and high prevalence of vector in the community. Increased incidence of complicated vivax malaria could be related to either recrudescence in the patients from original parasite or re-infections which could not be differentiated in area of continuous malaria transmission. Thus persistent exposure, changing clinical presentations and

complications associated with plasmodium vivax malaria can impose a significant burden of morbidity and mortality in children. Limitations of the present study were that sample size was small therefore results cannot be universalized.

## CONCLUSION

Clinical manifestations of plasmodium vivax infection ranged from asymptomatic to severe complications including cerebral malaria, acute renal failure, acute hemolytic crisis and hepatic dysfunction. Acute onset fever and hepatosplenmegaly were most common clinical manifestations found in 75% and 32.6% cases respectively. Anemia and thrombocytopenia were more frequent haematological parameters whereas leucopenia was less common in this study.

## RECOMMENDATIONS

Every child with acute febrile illness and systemic involvement should be investigated for complicated malaria. Further laboratory evidence of thrombocytopenia and severe anemia should raise suspicion of complicated vivax malaria in areas of high malaria endemicity.

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