P.Vivax Malaria: A Benign Disease with Emerging Complications

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Abstract- Background: Malaria is an endemic disease in India. It is a mosquito-borne infectious disease caused by genus Plasmodium. Complications usually occur with P.falciparum, its occurrence has been rarely reported in cases of P. vivax malaria. We observe 107 patients with P.vivax malaria who developed complications in the form of Thrombocytopenia, Acute kidney injury, hyperbilirubinemia & cerebral malaria, a rare presentation in P.vivax malaria.

Objectives: As the burden of P.vivax malaria is progressively increasing in community this study has been carried out to find out various complications in P.vivax malaria which is considered as a benign entity.

Methods: We prospectively enrolled 150 patients hospitalized in C.U.Shah hospital of P.vivax infection on initial microscopy with complications over a two year period. Hematological, biochemical, serological, radiological investigations are performed to identify complications.

Keywords: P.vivax malaria, complications of P.vivax, thrombocytopenia.

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Results: As per study, burden of P. vivax (67%) is more in community as compared to P. falciparum (33%). Out of 150 patients of P. vivax malaria, 107 patients were having various complications in the form of Thrombocytopenia (71.33%), Anemia (10%), hyperbilirubinemia (8.67%), Acute renal failure (8%) and cerebral malaria (1.33%) in their respective order. Most common complication is thrombocytopenia. Male gender is more prone to develop complicated P. vivax malaria than female with unknown reason.

Conclusion: As per observations, P. vivax malaria is no more benign disease. P. vivax can be presented with various complications and as far as thrombocytopenia is concern, it has a favorable prognosis and does not require platelet transfusion regularly except sequel is present.

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I. INTRODUCTION

Malaria is a mosquito-borne parasitic disease. In India it is mainly caused by P. vivax and P. falciparum. Complicated malaria characterized by serious organ failures or abnormalities in the patient’s blood or metabolism usually occurs in P. falciparum malaria. Manifestations of severe malaria include cerebral malaria, severe anemia, hemoglobinuria, ARDS, thrombocytopenia, cardiovascualr collapse and shock, acute kidney injury, metabolic acidosis and hypoglycemia.

In contrast to falciparum malaria, vivax malaria is rarely associated with serious complication. Scattered cases of P. vivax causing severe malaria have been reported in the last 30 years.

Manifestations of malaria vary from asymptomatic infection to severe malaria. The essential pathologic feature of severe malaria is sequestration of erythrocytes, which contain mature forms of the parasite in the deep vascular beds of vital organs and rosette formation, thus producing organ dysfunction.

P. vivax may no longer be a paradigm for uncomplicated malaria. Presence of thrombocytopenia in acute febrile travelers returning from tropical areas has become highly sensitive marker for malaria diagnosis (D’Acremont et al. 2002). The sensitivity of thrombocytopenia together with the acute febrile illness was 100% for malaria diagnosis, with specificity of 70%, a positive predictive value of 86% & a negative predictive value of 100% (Patel et al. 2004).

Since the beginning of the 1970s, there have been reports proposing that malaria associated thrombocytopenia is quite similar in P. vivax and P. falciparum infections (Beale et al. 1972). Most of the data were published in late 1990s because of an availability of affordable automated machines capable of performing complete blood count (CBC).

II. MATERIAL & METHODS

- This is a hospital based study conducted on the patients of the medicine department in C.U. SHAH medical college & hospital, Surendranagar (Gujarat) during July 2010 to July 2012.
  
  a) Inclusion Criteria
  - Patients who came in the outdoor dept. and/or admitted in medicine department with complicated P. vivax malaria.

  b) Exclusion Criteria
  - Patients who came in OPD and/or admitted in medicine dept. but do not have any type of complication of malaria.
  - Patients who are having only P. falciparum malaria or mixed infection of P. vivax & P. falciparum malaria.

  c) Diagnosis Of Malaria & Various Complications
  - Most of the diagnosis is made with the help of conventional study of thick and thin peripheral blood film.
  - Rapid antigen detection test is used and confirmed diagnosis, whenever required.
The complications of malaria are diagnosed mainly by various biochemical tests in pathology laboratory[ SIEMENCE auto analyzer] and chest x-ray.

III. Observation

- Total number of the P.vivax malarial cases observed within 2 years are 150. Out of them 43 cases are uncomplicated and 107 cases are of complicated P.vivax malaria.
- There are various complications in the form of Thrombocytopenia (71.33%), Anemia (10%), hyperbilirubinemia (8.67%), Acute renal failure (8%) and cerebral malaria (1.33%) in their chronological order have been observed in 107 cases of complicated P.vivax malaria.
- As shown in figure 1, out of 225 cases of malaria 150(66.66%) are of P.vivax and remaining 75(33.34%) of P.falciparum malaria.
- As shown in figure 2, the most common complication amongst all P.vivax malarial cases is THROMBOCYTOPENIA. After that Anemia > Jaundice > AKI > Cerebral malaria in their respective order.
- Thrombocytopenia with its sequel (hematuria, hemoptysis, hemetemesis etc.) is present only in few cases [2] & requires blood / platelet transfusion. Otherwise in all other cases thrombocytopenia remains silent without any sequel. So as such thrombocytopenia without any sequel is not a harmful condition.
- The criteria for diagnosis [3] of the complicated vivax malaria as follow…….
  - Thrombocytopenia - PLT < 150000/cumm
  - Anemia - Hb < 9.0gm/dl (severe anemia Hb < 5.0gm/dl)
  - Jaundice - serum billirubin > 2.5 mg%
  - Cerebral malaria – Glasgow coma scale 9/15
  - Renal failure - creatinine > 1.8mg%
- As discussed earlier, the most common form of complication is thrombocytopenia; Figure 3 is showing the different ranges of the thrombocytopenia occur in the malarial infection.
- As shown in figure 4, incidence of complicated P.vivax malaria in male is more than female. As such there is no any relation between gender and P.vivax infection[4].
- Age wise distribution (figure 5) is more amongst the people who are in between age group of 21 – 30 yrs. (38%) [Kocher et al]. Other age group distribution in the patients is uneven.
- Various forms of the parasite life cycle which have been observed in the peripheral blood film examination (figure 6). The TROPHOZOIT form followed by RING form is predominantly seen in the PBF study. The least common form of the parasite is GAMATOCYTE. While most of the time one or more types of the form of parasite are found together in the peripheral blood smear study.

IV. Discussion

- Organ dysfunction is characteristic of P.falciparum malaria & unusual in P.vivax infection. Severe complicated malaria is a well-recognized feature of P.falciparum malaria. Although a few cases with P.vivax have been reported in literature. Any patient infected with P. vivax who exhibits severe malaria is presumed to be suffering from mixed infection[5]. However, that may not be always true. As evident from the present report, P.vivax infection can also present with complications.
- Clinical data indicates that P.vivax can cause both sequestrations related and non-sequestration related complications of severe malaria [4]. The exact pathogenetic mechanism however remains elusive. Sachdev and Mohan [6] studied the clinicolaboratory profile of patients with P.vivax cerebral malaria. Focal neurological signs were observed in one patient. Recently a case of cerebral vivax malaria that presented with status epilepticus has been described [7].
- P.vivax malaria without any complication has been reported many times, even remains silent[8]. It may be presented occasionally with mild anemia or febrile illness. However, none of them had any evidence of thrombocytopenia, AKI and recovered without any sequel[8,9].
- However almost all type of complications have been found in this study, but more common one is thrombocytopenia.
- There are reports of thrombocytopenia occurring as a manifest of P.vivax malaria in adults. The mechanism of thrombocytopenia (figure 9) in malaria is not clearly known....
  1. Decreased thrombopoiesis, although this hypothesis was later ruled out [9,10]
  2. Thrombocytopenia is a result of peripheral destruction in which immune complexes generated by malarial antigens lead to sequestration of the injured platelets by macrophages in the spleen, although this mechanism has not been systematically evaluated in P.vivax malaria[1,11].
  3. An inverse relationship between elevated parasite levels and decreased platelet counts observation consistently has been reported for P.vivax infection[12].
- Fajardo and Tallent[9] in 1974 demonstrated P.vivax within platelets by electron microscopy and suggested a direct lytic effect of the parasite on the platelets. Both non-immunological destruction[13] as well as immune mechanisms involving specific platelet-associated IgG antibodies that bind directly to the malarial antigen in the platelets has been
recently reported to play a role in the lysis and the development of thrombocytopenia[14].

- Oxidative stress damage of thrombocytes has also been responsible based on the finding of low levels of platelet superoxide-dismutase and glutathione peroxidase activity and high platelet lipid peroxidation level in malaria patients, when compared to those of health subjects[15].

- Malaria may cause anemia and hyperbilirubinemia because of the loss of red blood cells. Intravascular hemolysis & DIC in P.vivax malaria can cause ARF, which occurs more in P.falciparum malaria but we found 8% cases in p.vivax infection[10] . Renal ischemia is the dominant pathogenic mechanism that results in acute tubular necrosis. The prognosis of ARF in P.vivax malaria is favorable.

V. Conclusion

- P.vivax may no longer be a paradigm for uncomplicated malaria. It has been observed that the burden of complicated P.vivax malaria is progressively increasing.
- Complications are common in the form of Thrombocytopenia(71.33%), Anemia (10%), hyperbilirubinemia(8.67%), Acute renal failure(8%) and cerebral malaria(1.33%) in their respective order. As far as the thrombocytopenia is concerned, it is having favorable prognosis & most of them were recovered with only antimalarial treatment so routine use of platelet transfusion is not recommended in a case of thrombocytopenia.
- P.vivax now a days emerging as one of the cause of isolated thrombocytopenia. It is a challenge to differentiate P.vivax from falciparum malaria and Dengue fever.

![Figure 1: Incidence of the P.Vivax Malaria](image)
Figure 2: Incidence of Complications of P. Vivax Malaria: A Benign Disease with Emerging Complications.
Figure 3: Incidence Of Severity Of Thrombocytopenia
Figure 4: Incidence Of P.Vivax In Male & Female Gender
Figure 5: Age Wise Distribution Of P. Vivax Malaria
**Figure 6**: Various Forms Of Lifecycle Of P.Vivax In Peripheral Blood Film

**Figure 7**: (Malarial Parasite Found In Rbc On Periferal Blood Smear Study)
Figure 8: (Man With Hyperbilirubinemia In P.Vivax Malaria)

Figure 9: Mechanisms Of Thrombocytopenia
REFERENCES Références Referencias