

CLINICAL PROFILE OF MALARIA WITH SPECIAL REFERENCE TO HEMATOLOGICAL AND RENAL ALTERATIONS

Basawaraj G. Mangshetty¹, Raghuram Bollineni², Satish T³

HOW TO CITE THIS ARTICLE:

Basawaraj G. Mangshetty, Raghuram Bollineni, Satish T. "Clinical Profile of Malaria with Special Reference to Hematological and Renal Alterations". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 22, March 16; Page: 3829-3836, DOI: 10.14260/jemds/2015/551

ABSTRACT: INTRODUCTION AND OBJECTIVES: Hematological and Renal alterations are seen mostly in Plasmodium falciparum infection, but P.vivax can occasionally contribute for renal, hematological impairment. Malarial ARF, Anemia, thrombocytopenia is commonly found in non-immune adults and older children with malaria. Occurrence of ARF, jaundice, anemia in severe malaria is quite common in Southeast Asia and Indian subcontinent. Several hypotheses including mechanical obstruction by infected erythrocytes, immune mediated glomerular and tubular pathology, and alterations in the renal microcirculation, lead to renal failure. **METHODOLOGY:** 220 patients were included in the study who are positive for malarial antigen and routine laboratory tests were like CBC, liver function tests, renal profile, peripheral smear were done at Basaveshwar Teaching and General Hospital, attached to Mahadevappa Rampure Medical College. **RESULTS:** 220 patients of malaria were analyzed. 60% had Plasmodium vivax, 34% had Plasmodium Falciparum and 6% had mixed infection. Complications of Plasmodium falciparum – Jaundice 47.5%, Anemia 27.5%, Renal failure 25%, Cerebral malaria 15%, ARDS 2.5%, Thrombocytopenia 5% and Hypoglycemia 5%. Complications of Plasmodium vivax - Jaundice 1.5%, Anemia 5.3%, Renal failure 6%. Cerebral malaria occurred in 2.7% of cases. Predominant presentations were altered behaviour, loss of consciousness, 28.5% of mixed malaria and 2.6% of PF patients had cerebral malaria. **INTERPRETATION AND CONCLUSION:** Malaria being a common infectious disease encountered in day to day practice, early recognition and prompt intervention of complications due to malaria is necessary. Mainstay of treatment consists of appropriate antimalarial drug therapy, fluid replacement, and renal replacement therapy if needed and correction of anemia, thrombocytopenia. **KEYWORDS:** Plasmodium vivax, plasmodium falciparum, anemia, thrombocytopenia, ARF.

INTRODUCTION: Malaria is probably one of the oldest diseases known to mankind that has had profound impact on our history. About 95% population in the country resides in malaria endemic areas and 80% of malaria reported in the country is confined to areas consisting 20% of population residing in tribal, hilly, and inaccessible areas. It continues to be a huge social, economic and health problem, particularly in the tropical countries.

WHO forecasts a 16% growth in malaria cases annually.^{1,2} About 1.5 million to 3 million people die of malaria every year (85% of these occur in Africa), accounting for about 4-5% of all fatalities in the world. Malaria ranks third among the major infectious diseases in causing deaths-after pneumococcal acute respiratory infections and tuberculosis.

Common clinical presentations of infection with all four Plasmodia species are periodic paroxysm, chills, rigors, sweating, body aches, headache, and prostration. Severe life-threatening complications such as cerebral malaria (CM), severe anemia, acidosis, respiratory distress, jaundice, acute renal failure (ARF), acute respiratory distress syndrome (ARDS), etc. occur mostly with P.

ORIGINAL ARTICLE

falciparum infection. A few reports have appeared indicating association of severe complications of malaria with *P. vivax* infection.^{3,4}

Hematological complication while seen both in *P. Falciparum* and *P. Vivax* malaria can become a serious and life threatening in *Falciparum* malaria. The reason for these being high level of parasitemia associated with *P. Falciparum*.

ARF is a frequent and serious complication of falciparum malaria in non-immune adults and older children.^{5,6} Malarial ARF has been reported from several European countries, where malaria transmission is virtually non-existent.^{7,8} Renal involvement in *P. vivax* malaria has been reported mostly from Indian subcontinent.⁹

Due to high incidence and mortality from complications in patients with malaria positivity, we have taken up this study to evaluate clinical, haematological and renal alterations in malaria patients proved positive.

OBJECTIVES OF THE STUDY:

- To study clinical, hematological and renal alterations in malaria patients proved positive by rapid optimal test and slide positivity in patients admitted to Basaveswara Teaching & General Hospital, Gulbarga.
- Comparing the severity of various clinical manifestations in *P. vivax* and *P. falciparum* malaria.
- To Compare and Evaluate various prognostic indicators like Thrombocytopenia, Anaemia, Renal failure, ARDS, Cerebral malaria and mortality in both *P. falciparum* and *P. vivax* malaria.

MATERIALS AND METHODS: A total of 220 patients diagnosed to have Malaria over a period of two years admitted in B.T.G.H attached to M.R.M.C included in the study. This is a prospective study. Patients with fever admitted to Basaveswara teaching and general hospital who were tested positive for plasmodium vivax /falciparum by peripheral smear study (Giemsa) / QBC (Quantitative Buffy Coat) were taken up for the study.

INCLUSION CRITERIA: All patients above 14 years of age and either sex whose blood smear positive for malaria are included in the study. All Patients are positive for malaria by ROT and Slide method.

EXCLUSION CRITERIA:

1. Clinical diagnosis of malaria without slide positivity and rapid optimal test.
2. Patients who received partial treatment outside hospital and referred to the hospital.
3. Patients with known HIV positive.
4. Patients with history of bleeding disorders, Oral anticoagulants.
5. Patients with history of renal failure.
6. Patients with history of chronic liver disease.
7. Patients with dengue and leptospirosis.

STATISTICAL METHODS: Chi square test or Fisher Exact test and student "T" test has been used to find the significant association of study characteristics (Thrombocytopenia) with type of malaria.

RESULTS: A total of 220 subjects who diagnosed to have Malaria over a period of two years were studied. The mean age of patients was 36.6±20.8 years. The study included 59.5% males and 40.5%

ORIGINAL ARTICLE

females. Typical fever with chills were observed in 132 patients of *P. Vivax* and 75 patients of *P. Falciparum*. Under atypical manifestations like vomiting was seen in 30 patients of *P. Falciparum* and 17 patients in *P. Vivax* 1 in mixed infection, headache in 33 patients of *P. Falciparum* and 30 in *P. Vivax*, jaundice in 24 patients of *P. falciparum*, 3 *P.vivax* and 5 mixed infection. Altered sensorium in 18 patients of *P. Falciparum* and 3 in *P.Vivax*, pain abdomen in 12 patients of *P. Falciparum* and 4 in *P. Vivax*. Commonest atypical symptom being headache and vomiting.

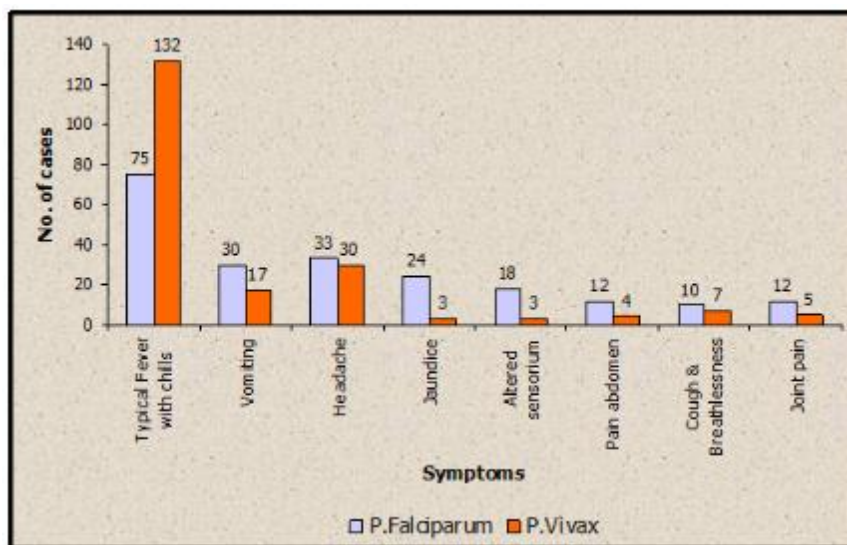


Fig. 1: Distribution of Symptoms

Common clinical sign in decreasing order are splenomegaly (42.7%), pallor (20.4%), Icterus (14.5. %), hepatomegaly (5.45%), altered sensorium (1.8%), petechial (5.4%).

Signs	Number of cases (n=220)	Percentage
Splenomegaly	94	42.7
Pallor	45	20.4
Icterus	32	14.5
Hepatomegaly	12	5.45
Hepatosplenomegaly	20	9
Altered sensorium	4	1.8
Petechia	12	5.4

Table 1: Distribution of signs

A total of 220 subjects who had malaria, 132 were *P.vivax* and 75 were *P.falciparum*. Incidence of *P.vivax* 60% and *P. falciparum* 34%.

Incidence of Thrombocytopenia was 116(52.27%). with mild Thrombocytopenia 46(20.8%), moderate Thrombocytopenia 46(21%) and 24(10.8%) with severe Thrombocytopenia. Normal platelet count was observed in 104(47.2%) of patients. Indicating thrombocytopenia is a common association in malaria.

ORIGINAL ARTICLE

Incidence of Thrombocytopenia	Number of cases (n=220)	Percentage
Above 1.5 lakh	104	47.2
1-1.5 lakh	31	14
50-1 lakh	15	6.8
20,000-50,000	46	21
10,000-20,000	19	8.6
Less than 10,000	5	2.2

Table 2: Incidence of thrombocytopenia

According to the revised WHO guidelines of 2000 patients who had Thrombocytopenia were grouped into complicated and uncomplicated. In complicated malaria 39 patients had Hemoglobin <5gm% in which 26(66%) were P.Falciparum and 7(17.9%) were P.Vivax, 36 patients had s.creatinine >3mg% in which 17(47.2%) were P.Falciparum and 8(22.2%) were P.Vivax, 30 patients had T.Bilirubin >3mg% in which 22(68.7%) were P.Falciparum and 2(6.75%) were P.vivax, 20 patients had metabolic acidosis (ph<7.2),14(70.%) were P.Falciparum and 2(10%) were P.Vivax,. 11 patients had spontaneous bleeding with DIC in which 8(72.7%) were P.Falciparum and 2(18.2%) in mixed, 6 patients had presented with altered sensorium in which 2(33.3%) were P.Falciparum and 4(66.7%) were mixed,

10 patients had hyperparasitemia in which 4 (50%) in P.Falciparum and 6 (60%) in mixed, 2 patients had hypoglycemia which was 2 (100%) mixed infection, 26 patients had prostration in which 12(46.1%) were P.Falciparum, 4(15.3%) P.Vivax and 10(38.9. %) mixed, 8 patients had ARDS in which 4(50%) were P.Falciparum and 4(50%) were mixed, 12 patients developed shock in which 4(33.3%) were P.Falciparum, 4(33.3%) were P.Vivax and 3(33.3%) were mixed.

Complications were commonly seen in P.falciparum and mixed compared to P.vivax of which anemia and hyperbilirubinemia being the most common.

Criteria	Number of patients	Species			P value
		P. Falciparum	P.Vivax	Mixed	
Hb<5 gm/dl	39	26 (66. %)	7 (17.9%)	6 (15.3%)	0.03
S.Creatinine >3mg%	36	17 (47.2%)	8 (22.2%)	11 (30.5%)	0.001
T.Bilirubin(>3 mg/dl)	32	22 (68.7%)	2 (6.75%)	8 (25%)	0.001
M. acidosis.ph<7.2	20	14 (70%)	2 (10%)	4 (20%)	0.05
Spt bleeding and DIC	11	8 (72.7%)	-	2 (18.2%)	0.01
Altered sensorium	6	2 (33.3%)	-	4 (66.7%)	0.8
Hyperparasitemia>5%	10	4(40.0%)	-	6 (60.0%)	0.07
B. sugar<40mg%	2	-	-	2(100.0%)	0.06
Prostration	26	12 (46.1%)	4 (15.3%)	10 (38.4%)	
ARDS	8	4 (50.0%)	-	4 (50.0%)	0.41
Systolic BP<80mmhg	12	4 (33.3%)	3 (33.3%)	5 (33.3%)	0.06

Table 3: WHO guidelines for complicated malaria

ORIGINAL ARTICLE

Mortality of 2.72% is noted. 2 patients had Falciparum and 4 mixed. The cause of death were cerebral malaria in one case and MODS in other three patients.

Species	Outcome		Number of patients
	Died	Recovered	
P. Falciparum	2 (2.66%)	73(97.3%)	75
P. Vivax	-	132(100.0%)	132
Mixed	4(30.7%)	9(69.2%)	13
Total	6 (2.72%)	214(97.2%)	220

Table 4: Mortality

DISCUSSION: A total of 220 malaria cases were studied in Basaveshwara Teaching & General Hospital, Gulbarga. The mean age of the patients were 36.6+20.81.¹⁰ older age groups are susceptible to infection due to lack of immunity. This study includes 136 male and 89 female patients. In the present study males are commonly involved due to the fact that most of the patients had recent history of travel to endemic areas.^{10,11} The commonest clinical manifestation were fever with chills and rigors (100%), headache (33%), vomiting (21.2%), jaundice (13.5%).¹² Commonest sign being splenomegaly (42.7%) followed by pallor (22.4%) and icterus (14.5%). A clinical spectrum of fever, splenomegaly and pallor is always associated with malaria.

Out of 220 cases 131 had P.vivax malaria, 75 patients had P.falciparum, and 4 had mixed infection. Incidence of P.vivax malaria is 60% and P.falciparum 34%. Prevalence of P.vivax malaria is common in India, because of variation in climatic condition, breeding places of mosquito and genetic resistance of P.falciparum.

It is reported in following studies (Values in percent) Jaundice is one of the commonest complications noted in our study. Serum bilirubin of more than 1.5mg occurred in 32 cases (14.5%). Serum Bilirubin ranged from 1.5 to 12mg/dl. Bilirubinemia is predominantly direct. Jaundice occurred in 6.75% of PV and 68.7% of PF cases. This is consistent with a study from Calcutta, in which hazra et al reported jaundice in 9.09% of PV and 40% of PF cases. Harris VK et al from south India reported 37% of jaundice in Pf cases.¹³ Bilirubinemia is predominantly direct and in most of the cases there is only mild elevation of transaminases.

The cause of jaundice is due to increased intravascular hemolysis of parasitized erythrocyte, hepatic dysfunction and rarely micro angiopathic hemolysis due to disseminated intravascular coagulation.

RENAL FAILURE: Acute renal failure occurred in 16.3% of cases (Serum Creatinine >1.5mg/dl). In our study ARF occurred in 22.2% of PV and 47.2% of PF cases. This is consistent with Kochar's reported incidence of 6.25% of ARF in PF cases in 2001.¹⁴ Nityanand et al reported an incidence of 21% ARF in a study of 60 cases (PV 14 and PF 46). In our study it has been found that renal failure also occurs in PV malaria in significant numbers. This has been proved by Kochar in his study of complicated Vivax malaria by documenting presence of PV and absence of PF by genetic study (PCR).

One patient with ARF died who also had other complications like jaundice, Anemia and ARDS. In India reported incidence of ARF in malaria is 17.8% from Delhi, 17.2% from Orissa, 13% from Northeast India and 5.9% from Mumbai.

ORIGINAL ARTICLE

ANEMIA: 39 (17.7%) patients had Hb <5g/dl. The lowest Hb noted in our study was 2.3g/dl. 5.3% of PV and 34.6% of PF cases had Hb <5g/dl. This is consistent with Kochar's reported incidence of severe anemia in 26.04% of PF cases.¹⁴

THROMBOCYTOPENIA: In this study 114 subjects out of 220 malaria cases had thrombocytopenia. Incidence of thrombocytopenia being 51.8%. Thrombocytopenia is a common feature of acute malaria and occurs in both *P.falciparum* and *P.vivax* infection regardless of severity of infection. Thrombocytopenia in a patient with febrile illness increases the possibility of malarial infection.

The mechanism of thrombocytopenia is uncertain. Immune mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been postulated. Abnormalities in platelets structure and function have been described as a consequences of malaria, and in rare instances platelets can be invaded by malarial parasite themselves.¹⁵

ARDS developed in 8(3.6%) patients, 4(1.8%) in mixed malaria and 4(1.8%) in PF. Kochar reported 3.01%of ARDS in PF cases in 2001.

Algid malaria with profound hypotension occurred in 12 cases, 3(33.2)% in PV and 4(33.3%) in PF. Kochar reported 5.26% of shock in PF cases in 2001.

The WHO criteria for diagnosis of organ dysfunction in severe malaria is serum Creatinine and Bilirubin of more than 3 mg / dl. We had taken a criteria of > 1.5 mg/dl for early diagnosis of ARF and jaundice which would prompt aggressive management early and prevent mortality.

Six patients died which accounts for 2.7% of mortality rate. 2 had PF and 4 had mixed. One patient with PF died of cerebral malaria and all the other five deaths were due to MODS with ARDS and underlying chronic illness. This is consistent with Kochar's findings of shift in cause of mortality from cerebral malaria to MODS (1994 to 2001). Low mortality may be due to early detection of organ dysfunction and aggressive management.

CONCLUSION:

- 220 patients of malaria were analyzed. 132 (60%) had *Plasmodium vivax*, 75 (34%) had *Plasmodium Falciparum* and 13(6%) had mixed infection.
- Complications of PF (n – 40) – Jaundice 47.5%, Anemia 27.5%, Renal failure, 25%, Cerebral malaria 15%, ARDS 2.5%,Thrombocytopenia 5% and Hypoglycemia 5%.
- Complications of PV (n – 132) - Jaundice 1.5%, Anemia 5.3%, Renal failure 6%.
- Jaundice occurred in 1.5% of PV and 29.3% of PF cases, with predominantly elevation of direct bilirubin with mild elevations of transaminases in the range of 40 to 80 IU/L. This shows that jaundice in malaria is predominantly of cholestatic in origin.
- Renal failure occurred in 6% of PV and 22.6% of PF cases. Overall renal failure occurred in 16.3% of malaria.
- 39 patients had Hb <5g/dl. 5.3% of PV and 34.6% of PF had Hb <5g/dl.
- Cerebral malaria occurred in 2.7% of cases. Predominant presentations were altered behaviour, loss of consciousness, 28.5% of mixed malaria and 2.6% of PF patients had cerebral malaria.
- Other complications are less common. They were ARDS 5.3%, Hypoglycemia 0.9%,and 5.4% of hypotension with shock

ORIGINAL ARTICLE

- 42.4% of patients with *P.vivax* malaria were treated with chloroquine, followed by radical cure and 58% were treated with quinine in non-responders.
- Artemisinin group of drugs used in all patients of falciparum and mixed infections and some cases responded to artemether and lumefantrine combination therapy and few others responded to clindamycin.
- Mortality – six patients (2.7%) died, two (1.4%) in falciparum and four (2.5%) in mixed malaria. Multiple organ dysfunction syndrome was the cause of death in five out of six patients and one died of underlying coronary artery disease.

REFERENCES:

1. WHO Expert Committee on malaria; Twentieth report 1998. Geneva, Switzerland 2000.
2. National Anti-Malaria Program. New Delhi: Directorate of NAMP, Ministry of Health and Family welfare 2002.
3. Kumar S, Melzer M, Dodds P, Watson J, Ord R. *P. vivax* malaria complicated by shock and ARDS. *Scand J Infect Dis* 2007; 39: 255–6.
4. Kochar DK, Saxena V, Singh N, Kochar SK, Vijay Kumar S, Das A. *Plasmodium vivax* malaria emerging infectious diseases. www.cdc.gov/eid. V 11, No. 1, January 2005.
5. Eiam-Ong S, Sitprija V. Falciparum malaria and the kidney model of inflammation. *Am J Kidney Dis* 1998; 32: 361–75.
6. Eiam-Ong S. Malaria nephropathy. *Seminars in Nephrology* 2003; 23: 21–33.
7. Losert H, Schmid K, Wilfing A, Winkler S, Staudinger Kletzmayer J, et al. Experiences with severe *P falciparum* malaria in the intensive care unit. *Intensive Care Med* 2000; 26: 195–201.
8. Gerritsen JG, van der Zwan JC. Acute renal failure in severe chloroquine resistant falciparum malaria. *Intensive Care Med* 1992; 18: 177–9.
9. Mehta KS, Halankar AR, Makwana PD, Torane PP, Satija PS, Shah VB. Severe acute renal failure in malaria *J Postgrad Med* 2001; 47: 24–6.
10. Kochar DK, Subhakaran, BL Kumawat et al. Cerebral malaria In Indian Adults; *JAPI* 2002; 50:234-241.
11. Sitprija V. Nephropathy in falciparum malaria. *Kidney Int* 1988; 34: 867–77.
12. Prakash J, Tripathi K, Malhotra et al. Acute Renal Failure in eastern India. *Nephrol Dial Transplant* 1995; 10:2009 – 2012.
13. Mehta KS, Halankar AR, Makwana PD et al. Severe Acute Renal Failure In Malaria. *J Post Grad Med* 2001; 47: 24-6.
14. DK Kochar & Naresh Rawat. Myriads of Presentation of Falciparum Malaria. *Medicine update*; 13: 136-40.
15. Choi HJ, Lee SY, Yang H, Bang J K "Retinal haemorrhage in vivax malaria". *Trans R Soc Trop Med Hyg.* 2004 Jun; 98(6): 387-9.

ORIGINAL ARTICLE

AUTHORS:

1. Basawaraj G. Mangshetty
2. Raghuram Bollineni
3. Satish T.

PARTICULARS OF CONTRIBUTORS:

1. Professor, Department of General Medicine, MRMC, Gulbarga.
2. Post Graduate, Department of General Medicine, MRMC, Gulbarga.
3. Post Graduate, Department of General Medicine, MRMC, Gulbarga.

FINANCIAL OR OTHER

COMPETING INTERESTS: None

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Raghuram Bollineni,
Room No.105,
Basaweshwar PG Boys Hostel,
Sedam Road, Gulbarga-585105, Karnataka.
E-mail: raghuram.bollineni@gmail.com

Date of Submission: 18/02/2015.
Date of Peer Review: 19/02/2015.
Date of Acceptance: 04/03/2015.
Date of Publishing: 14/03/2015.