RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 4 | April 2015 | ISSN - 2249-555X

Vivax Malaria - do we Under Rate it?

KEYWORDS: Vivax malaria , P.Vivax, Thrombocytopenia, Anaemia

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ABSTRACT *Background : While research on P. vivax is scarce because it is considered benign, it has become evident with implementation of molecular diagnosis that it can also cause multiple organ dysfunction and severe life-threatening disease.*

Objective: This study aimed to synthesize the evidence on severe malaria in P. vivax infection compared with that in P. falciparum infection

Materials and methods :This prospective study was conducted on 680 patients detected positive for malaria at Shishu hospital (private), catering to a large rural area in and around Chandrapur and neighboring area of Wardha and Gadchiroli district. The detailed clinical history and physical examination of the patient at the time of admission was done in a standard proforma. Investigations like haemoglobin, complete blood count (CBC), peripheral smear, para-check were done

Result:Out of the 680 patients screened positive for malaria 472 were positive were P.vivax and 208 for P.falciparum. The most common presentation was anemia followed by convulsions and thrombocytopenia which was more severe in patients with P.vaivax malaria.

Conclusion. The study stresses that Plasmodium vivax can result in severe disease and can no longer be considered a benign condition and that some manifestations such as leukopenia and thrombocytopenia which are not part of WHO severity criteria were frequently present and were associated with severe malaria.

INTRODUCTION:

Malaria is caused by protozoan parasites of genus *Plasmodium* and is transmitted to humans by *Anopheles spp.* mosquitoes. There are five species of plasmodium that cause disease in humans; *P. falciparum, P. vivax, P. malariae, P. ovale* and *P. knowlesi. (P. knowlesi* is usually restricted to monkeys in South East Asia, but has been identified as a cause of malaria in humans) [1].

Malaria is endemic in more than 100 countries worldwide where approximately 3.4 billion people are exposed to the disease [2]. India alone contributes 80% of south east Asia malaria burden. [3]

The signs and symptoms of malaria typically begin 8–25 days following infection[4] however, symptoms may occur later in those who have taken antimalarial medications as prevention.[5] Initial manifestations of the disease—common to all malaria species—are similar to flu-like symptoms,[6] and can resemble other conditions such as septicemia, gastroenteritis, and viral diseases.[5] The presentation may include headache, fever, shivering, joint pain, vomiting, hemolytic anemia, jaundice, hemoglobin in the urine, retinal damage, and convulsions.[7]

The classic symptom of malaria is paroxysm—a cyclical occurrence of sudden coldness followed by shivering and then fever and sweating, occurring every two days (tertian fever) in P. vivax and P. ovale infections, and every three days (quartan fever) for P. malariae. P. falciparum infection can cause recurrent fever every 36–48 hours or a less pronounced and almost continuous fever.[8]

Severe malaria is usually caused by P. falciparum (often referred to as falciparum malaria). Symptoms of falciparum malaria arise 9–30 days after infection.[5] Individuals with cerebral malaria frequently exhibit neurological symptoms, including abnormal posturing, nystagmus, conjugate gaze palsy (failure of the eyes to turn together in the same direction), opisthotonus, seizures, or coma.[5]

WHO had given guidelines for severe malaria.[9]

Initial World Health Organization Criteria from 1990

(i)Cerebral malaria: unarousable coma nonattributable to any other cause, with a Glasgow Coma Scale score ≤9. Coma should persist for at least 30 min after generalized convulsions.(ii)Severe anemia: hematocrit <15% or hemoglobin <50 g/L in the presence of parasite count >10 000/μL.(iii)Renal failure: urine output <12 mL/kg/24 hours in children and a serum creatinine>3.0 mg/dL despite adequate volume repletion.(iv)Pulmonary edema and acute respiratory distress syndrome.(v)Hypoglycemia: whole blood glucose concentration <40 mg/dL.(vi)Circulatory collapse (algid malaria): systolic blood pressure <70 mmHg in patients >5 years of age (<50 mmHg in children aged 1.5 years), with cold clammy skin or a core-skin temperature difference >10°C.(vii)Abnormal bleeding and/or disseminated intravascular coagulation: spontaneous bleeding from gums, nose, and gastrointestinal tract, or laboratory evidence of disseminated intravascular coagulation.(viii)Repeated generalized convulsions: 3 convulsions observed within 24 hours.(ix)Acidemia/acidosis: arterial pH <7.25 or acidosis (plasma bicarbonate <15 mmol/L).(x)Macroscopic hemoglobinuria: hemolysis not secondary to glucose-6-phosphate dehydrogenase deficiency.

Added World Health Organization Criteria from 2000

(i)Impaired consciousness: arousable mental condition.(ii) Prostration or weakness.(iii)Hyperparasitemia: >5% para-

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sitized erythrocytes or >250,000 parasites/μL (in nonimmune individuals).(iv)Hyperpyrexia: core body temperature >40°C.(v)Hyperbilirubinemia: total bilirubin >2.5 mg/dL.

Plasmodium vivax is one of the major species of malaria infecting humans. Although emphasis on *P. falciparum* is appropriate, the burden of vivax malaria should be given due attention. This study aimed to synthesize the evidence on severe malaria in *P. vivax* infection compared with that in *P. falciparum* infection

MATERIAL AND METHOD:

This longitudinal study was conducted on 680 patients detected positive for malaria at Shishu hospital (private), which is a 60 bedded hospital, catering to a large rural area in and around Chandrapur and neighboring area of Wardha and Gadchiroli district which is a tribal area.

Study design:Longitudinal study of 1 year duration (April 2012- April 2013)

Inclusion criteria:

All patients admitted to hospital during the study period with the complains such as:

- High grade fever with chills and /or rigors
- Fever and convulsions
- Fever and altered consciousness
- Fever and shock
- Tested positive for malaria were included in the study.

Exclusion criteria

Patients who were suspected with malaria but where proved negative on laboratory investigation.

The detailed clinical history and physical examination of the patient at the time of admission was done in a standard proforma.Investigations like haemoglobin, complete blood count (CBC), peripheral smear, para-check were done. Other blood investigations like LFT, KFT, LPand neuro-imaging were done as and when indicated.

Hemoglobin and platelet count was done by cell-counter-Merck Medonics method. Thick and thin smear for malaria was also done. A drop of blood was used for a thin blood film and stained with Leishman's stain. At least 100 high-power thin film microscopic fields were examined to diagnosis malaria. Plasmodium species were identified on the thin film and confirmed by a senior pathologist. Study of the antigen was done by J.Mitra method (rapid detection test)

The clinical course of these patients was monitored for any complications during the hospital stay.

OBSERVATION AND RESULT:

Table I: Total number of patients in Private hospital:

	Total number of patients	Total suspected for malaria	Total positive for malaria
Male	2512	853	452 (66.4%)
female	1177	677	228 (33.5%)
total	3689	1530	680

Out of 3689 patients who visited the private hospital duringApril 2012- April 2013, 1530 patients were suspected having malaria out of which 853 (55.75%) were male and 677 (44.2%) were females.Out of these, Leishman stain was positive for 680 patients, 452 (66.4%) being male and 228 (33.5%) being female.

Table II : Distribution of cases according to type of specie involved

	P.VIVAX		P.FALCIPARUM	
	NO.	%	NO.	%
Total no of cases-680	472	69.4	208	30.6

A total of 680 patients with malaria were admitted during study period, of which 472 (69.4 %) patients had P. Vivax and 208 (30.6 %) patients had P. falciparum malaria.

There were no cases involving both the species at the same time.

Table III: Age-wise distribution of malaria

Age group	P.Falciparum		P.Vivax	
	Number	%	Number	%
<5 years	62	31.25	142	30.08
5-10 years	75	36.05	157	33.26
10-15 years	71	34.13	172	36.44
Total	208	100	472	100

Out of the positive 680 patients, maximum patients belonged to the age group of 5-10 years (36%) in case of patients suffering from P. Falciparum and 36.4% patients belonged to the age group of 10-15 years in case of P.Vivax

Table IV: Peripheral blood smear for Malarial Parasite

	Number	%
P.Falciparum	153	22.5
P.Vivax	366	53.82
P.Falciparum and P.Vivax	98	14.41
Negative	63	9.26
Total	680	100

P. Falciparum was found positive in 153 slides of peripheral blood smear and P.vivax was positive in 366 slides whereas 98 peripheral blood smear slides showed both the species.

Table V : Distribution of cases on basis of complications

	P.VIVAX		P.FALCIPARUM	
	NO.	%	NO.	%
Convulsion within 48hrs	130	27.5	62	29.8
Hb% less than 6gm/dl	178	37.7	71	34.1
Thrombocytopenia less than 1lac	67	14.2	54	25.9
Uncomplicated	97	20.5	21	10

Convulsions were present in 62 patients (29.8%) with falciparum and 130 patients (27.5%) with vivax malaria.

Thrombocytopenia was present in 67 patients (14.2%) with vivax and 54 patients (25.9%) with falciparum malaria.Severe anemia was not uncommon.

Volume : 5 | Issue : 4 | April 2015 | ISSN - 2249-555X

Graph I : Clinical and hematological complications in both species of plasmodium

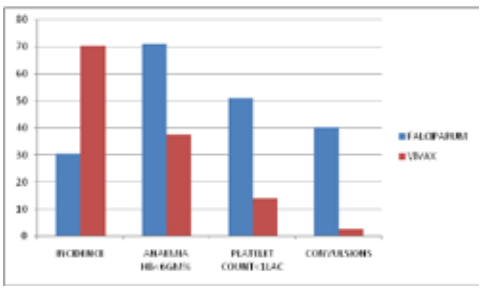

Table VI: Diagnosis by Rapid Detection Test

	Number	%
P.Falciparum	189	27.79
P.Vivax	418	61.47
Negative	73	10.73
Total	680	

Rapid detection test was conducted out of which 189 positive results were found of P.Falciparum and 418 of P.vivax whereas 73 negative results were seen.

TREATMENT:
Patients were initially treated with Chloroquine in standard doses. Those patients who did not have a satisfactory initial response to Chloroquine were treated with Quinine sulphate in standard doses. Blood sample for platelet count was repeated on fifth day and tenth day from start of antimalarial therapy to check the recovery of platelet counts.

DISCUSSION:
Malaria is a common infection in most parts of India and is commonly associated with mild thrombocytopenia [10].

Traditionally, severe malaria has been associated with infections due to P.Falciparum. Recent studies from South-East Asia have highlighted P.Vivax as a major cause of morbidity and mortality in infants and children [11,12]

In places where both P.Vivax and P.Falciparum co-exist, measures need to be equally targeted to P.Vivax to decrease morbidity and mortality due to severe malaria.

In July 2013, a total of 365193 malaria cases have been detected in India, of which there were 123 deaths. In Maharashtra there were a total of 22,822 malaria cases with 28 deaths. Maximum number of cases were in Orissa and minimum in Delhi. [13]

In present study, a total of 1530 patients with clinical suspicion of malaria were screened, using RDTs and peripheral smear, from April 2012- April 2013 and 850 patients were excluded due to both peripheral smear and RDT negative. 680 cases with proved malaria were included in study out of which 472 (69.4%) were Plasmodium vivax and 208 (30.6%) were Plasmodium Falciparum .

In study of Kaushik JS *et al* out of 1680 children screened for malaria, 38 children with proved malaria were included in study out of which 35 (92.1%) were due to Plasmodium vivax and remaining 3 (7.9%) were due to Plasmodium falciparum infection.[14]

Profound thrombocytopenia is a well-recognized complication of falciparum malaria but has been less well described in vivax malaria. Of 173 cases of malaria in U.S. Soldiers reported by Martelo et al [15] in 1969, 93% had malaria with *P. Vivax* but only 15% had thrombocytopenia with however no documentation of the lowest platelet count.

In Horstmann's series [16] the lowest count in 39 cases of vivax malaria was $44x10^9$/L. Pukrittayakamee et al. [17] described a case of a volunteer experimentally infected with the Chesson's strain of *P. Vivax* with a platelet count of $20x10^9$/L.

Thrombocytopenia is a common feature of acute malaria and occurs in both P.Falciparum and P.vivax infections regardless of severity of infection. Thrombocytopenia is rarely accompanied by clinical bleeding or biochemical evidence of DIC. Platelet count can fall to below 25000, but this is uncommon [18]

In present study, thrombocytopenia was present in 67 (14.2%) cases of P.vivax and 119 (57.2%) cases of P.Falciparum but none of them had bleeding anifestations. It was observed that incidence of thrombocytopenia was similar with P.Vivax and Falciparum infection (36.8 and 34.2% resp). Sarkar *et al.* in their study of 200 patients found that thrombocytopenia was present in 120 (60%) of patients and severe thrombocytopenia in 24 (12%) of patients [19]

In the study of Jadhav et al. platelet count less than 1.5 lac was noted in 79.4% of 1565 patients [20]. Gupta et al found that amongst 130 patients with P.Vivax malaria 100 had thrombocytopenia and 90 patients with P.Falciparum malaria 70 had thrombocytopenia [21]

Clinical data provided by Kochar, et al. indicates that P. vivax can cause both sequestration related and non-sequestration related complications of severe malaria, all of which are commonly associated with P. falciparum infections[22]. The exact pathogenetic mechanism however remains elusive.

Sachdev and Mohan[23] studied the clinico-laboratory profile of six patients with vivax cerebral malaria. The presenting features were of an acute febrile encephalopathy, convulsions and coma. Focal neurological signs were observed in one patient. Ozen, et al.[24] have recently described a case of cerebral vivax malaria that presented with status epilepticus

CONCLUSION:
The present study highlights the epidemiology of P. vivax malaria. Since P. vivax was considered a benign disease, there are scarce reports. The study stresses that Plasmodium vivax can result in severe disease and can no longer be considered a benign condition. The present study shows that some manifestations renal impairment, hypoglycemia, jaundice, and hyperparasitema were not seen, whereas leukopenia and thrombocytopenia which are not part of WHO severity criteria were frequently present and were associated with mortality.

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REFERENCE

1. Cox-Singh J, Singh B. Knowlesi malaria: newly emergent and of public health importance? Trends Parasitol. 24:406-10, 2008. | 2. World Health Organization. World Malaria Report 2013. | 3. WHO, World Malaria Report 2013, World Health Organization, Geneva, Switzerland, 2013. | 4. Fairhurst RM, Wellems TE (2010). "Chapter 275.Plasmodium species (malaria)". In Mandell GL, Bennett JE, Dolin R (eds). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases 2 (7th ed.). Philadelphia, Pennsylvania: Churchill Livingstone/Elsevier. pp. 3437–62. ISBN 978-0-443-06839-3. | 5. Nadjm B, Behrens RH (2012). "Malaria: An update for physicians". Infectious Disease Clinics of North America 26 (2): 243–59.doi:10.1016/j.idc.2012.03.010. PMID 22632637. | 6. Bartoloni A, Zammarchi L (2012). "Clinical aspects of uncomplicated and severe malaria". Mediterranean Journal of Hematology and Infectious Diseases 4 (1):e2012026. doi:10.4084/MJHID.2012.026.PMC 3375727. PMID 22708041. | 7. Beare NA, Taylor TE, Harding SP, Lewallen S, Molyneux ME (2006). "Malarial retinopathy: A newly established diagnostic sign in severe malaria". American Journal of Tropical Medicine and Hygiene 75 (5): 790–7.PMC 2367432. PMID 17123967. | 8. Ferri FF (2009). "Chapter 332. Protozoal infections".Ferri's Color Atlas and Text of Clinical Medicine. Elsevier Health Sciences. p. 1159. ISBN 978-1-4160-4919-7. | 9. WHO, World Malaria Report 2013, World Health Organization, Geneva, Switzerland, 2013. | 10. Looareesuwan S., Davis J.G., Allen D.L., et al. Thrombocytopenia in malaria. Southeast Asian J Trop Med Public Health 1992;23:44 | 11. Poespoprodjo JR, Fobia W, Kenangalem E, et al. Vivax malaria, a major cause of morbidity in early infancy. Clin Infect Dis 2009;48:1704-12 | 12. Genton B, D'Acremont V, Rare L. et al. Plasmodium Vivax and mixed infections are associated with severe malaria in children: a prospective cohort study from Papua New Guinea. PLoSNegl Trop Dis Negl Trop Dis Med 2008; 5:e127 | 13. National vector borne disease control programmed. Directorate General of health services. Ministry of Health and Family Welfare Available at URL:http://www.nvbdcp.gov.in.(Cited on 2011 aug 22) | 14. Kaushik JS et al. Severe malaria among children in Delhi. J Health PopulNutr 2012 Mar;30(1):113-116 | 15. Martelo O.J., Smoller M., Saladin T.A. Malaria in American soldiers. Arch Int Med 1969;123:383-7 | 16. Horstmann R.D., Dietrich M., Bienzle U., Rasche H. Malaria induced thrombocytopenia. Blood 1991;42:157-64. | 17. Pukrittayakamee S., White N.J., Clemens R. ,etal.Activation of the coagulation cascade in falciparum malaria. Trans R Soc Trop Med Hyg 1989;83:762-6 | 18. Sharma SK, Das RK, Das BK, Das PK. Haematological and coagulation profile in acute falciparum malaria. J Assoc Physicians India 1992;40:5811-3 | 19. Sarkar D, Ray S, Saha M, Chakraborty A, Taluldar A. Clinico-laboratory profile of severe Plasmodium Vivax malaria in tertiary care centre in Kolkata. Trop parasitol 2013;3:53-7 | 20. Jadhav UM, Patkar VS, Kadam NN. Thrombocytopenia in malaria: Correlation with type and severity of malaria. J.Assoc Physicians India. 2004;52:615-8 | 21. N.K.Gupta, SB Bansal, UC Jain, K.Sahare. Study of thrombocytopenia in patients of malaria. Trop Parasitol.2013 Jan-Jun;3(1):56-61 | 22. Kochar DK, Saxena V, Singh N, Kochar SK, Kumar SV, Das A. Plasmodium vivax malaria. Emerg Infect Dis 2005; 11: 132-134. | 23. Sachdev HPS, Mohan M. Vivax cerebral malaria. J Trop Pediatr, 1985; 31: 213-215 | 24. Ozen M, Gungor S, Atambay M, Daldal N. Cerebral malaria owing to Plasmodium vivax: case report. Ann J Pediatr 2006; 26: 141-144. |