ORIGINAL ARTICLE

JIACM 2018; 19(4): 274-77

Complications in Malaria Patients: Comparison between *P. vivax* and *P. falciparum*

Chhaya Mittal, Sandhya Gautam**, Gajraj Singh***, Ayush Agarwal*****

Abstract

Background: Malaria is one of the leading causes of morbidity and mortality in tropical countries. Plasmodium vivax causes benign malaria with a low incidence of complications as compared to Plasmodium falciparum. We have compared the complications in vivax malaria with those in falciparum malaria.

Aim: To study the complications between P. vivax and P. falciparum malaria at a tertiary care centre in Meerut, India.

Material and methods: This retrospective cross-sectional study was conducted at L.L.R.M. Medical college and associated S.V.B.P Hospital, Meerut from the month of July 2015 to December, 2015. All malaria patients (P. vivax, P. falciparum and mixed, i.e., both vivax and falciparum) who were admitted to our hospital were included in this study. These patients were positive on rapid malaria antigen test and peripheral blood smear.

Results and analysis: 64 cases of malaria were included, Out of these 50 were P. vivax positive, 10 were P. falciparum positive and 4 were positive for both. The complications seen in vivax malaria patients were; thrombocytopenia (24%), anaemia (60%), encephalopathy (2%), acute kidney injury (4%), jaundice (32%) and hypoglycaemia (6%), while 50% of falciparum patients manifested with jaundice and anaemia, 10% developed encephalopathy and hypoglycaemia and thrombocytopenia was seen in 20%.

Conclusion: Complications seen in falciparum malaria were also frequently observed in vivax malaria. Patients of vivax malaria should be monitored for occurrence of different complications. Severe vivax malaria is a relatively new and developing hazard.

Key words: Malaria, P. falciparum, P. vivax, anaemia, encephalopathy, acute kidney injury, jaundice, hypoglycaemia.

Introduction

According to the WHO estimates released in December 2015, there were 214 million cases of malaria in 2015 and 4,38,000 deaths[1]. Malaria is caused by plasmodium parasites, which infect humans by the bite of infected female anopheles mosquitoes, called "malaria vectors". There are 5 parasite species that cause malaria in humans; they are *P. vivax*, *P. falciparum*, *P. ovale*, *P. malariae*, *P. knowlesi* [2]. Two out of these, i.e., *P. falciparum* and *P. vivax* pose the greatest threat.

P. falciparum is known to cause severe complications such as cerebral malaria, severe anaemia, renal failure, pulmonary oedema and acute respiratory distress syndrome, hypoglycaemia, circulatory collapse, abnormal bleeding and/or disseminated intravascular coagulation, repeated generalised convulsions, acidaemia/acidosis, and macroscopic haemoglobinuria[2]. However, recently it has been observed that *P. vivax* can also cause complicated malaria.

Aim

To compare the complications and their rates between *P. vivax* and *P. falciparum* malaria patients at a tertiary care centre in North India.

Materials and method

This retrospective cross-sectional study was conducted at L.L.R.M. Medical College and associated S.V.B.P Hospital, Meerut from the month of July 2015 to December, 2015. All malaria patients (*P. vivax*, *P. falciparum* and mixed, i.e., both *vivax* and *falciparum*) who were admitted to our hospital were included in this study. These patients were positive on rapid malaria antigen test and peripheral blood smear. The record of these patients related to various complications was obtained from case notes. Data compilation was done. A comparison of complications between vivax and falciparum malaria was done and statistically significant differences were checked by using chi-square test which was considered significant at a level of $p < 0.05$.

Observation

In the study a total of 64 malaria patients were admitted in the SVBP Hospital. Out of 64 patients, 34 were males and

Associate Professor, Department of Community Medicine, **Associate Professor, ****Junior Resident III, Department of Medicine, ***Associate Professor, Department of Orthopaedics, LLRM Medical College, Meerut - 250 004, Uttar Pradesh.
Corresponding Author: Dr Sandhya Gautam, Associate Professor, Department of Medicine, LLRM Medical College, Meerut - 250 004, Uttar Pradesh. Tel: 9720524489, E-mail: sandyg.3080@gmail.com.

30 were females.

In this study of 64 malaria patients, 50 were *P. vivax* positive, 10 were *P. falciparum* positive, and 4 were positive for both *P. vivax* and *P. falciparum*. It shows that *P. vivax* was more prevalent in the community. All patients were studied for various complications such as anaemia, jaundice, acute kidney injury, hypoglycaemia, thrombocytopenia and encephalopathy.

When prevalence of anaemia was studied, it was observed that 39 patients (60.9%) were anaemic. When difference between males and females was studied almost all the females were anaemic (96.7%), while 29.4% males were anaemic.

When difference between *P. vivax* and *P. falciparum* malaria patients was analysed, 60% of *vivax* positive patients were anaemic, while anaemia was present among 50% of *falciparum* positive patients and it was 100% among patients of mixed infections. But this difference was not statistically significant.

When occurrence of jaundice was studied, it was seen in 23 (35.9%) patients. Among *P. vivax* positive patients 32% developed jaundice while 50% of *P. falciparum* developed jaundice. Among those who were having dual infection 50% were jaundiced. (P value > 0.05) This difference between *vivax* and *falciparum* was in-significant.

In our study, thrombocytopenia was seen in 16 patients. Out of total *P. vivax* positive patients 24% developed thrombocytopenia while 20% of *P. falciparum* positive patients developed thrombocytopenia. 50% of patients with both *falciparum* and *vivax* positive developed this complication. (P value > 0.05). The difference was not significant.

In the present study, acute kidney injury was seen in 2 patients and both were *P. vivax* positive. 4% of *P. vivax* positive patients developed acute kidney injury while none among *falciparum* and mixed infections (P value > 0.05).

Encephalopathy was seen in 3.1% of patients. Among *P. falciparum* positive patients 10% developed encephalopathy, while only 2% of *P. vivax* positive patients developed encephalopathy. This difference in occurrence of encephalopathy was not found to be significant (p > 0.05).

In our study, hypoglycaemia was seen in 4 patients (6.25%). 6% of *P. vivax* positive patients and 10% of *P. falciparum* positive patients developed this complication (P value > 0.05). The difference was found to be insignificant.

In our study, no patient developed ARDS and rupture of spleen, which has been reported as a significant cause of death. None of the admitted malaria patients died during the course of treatment.

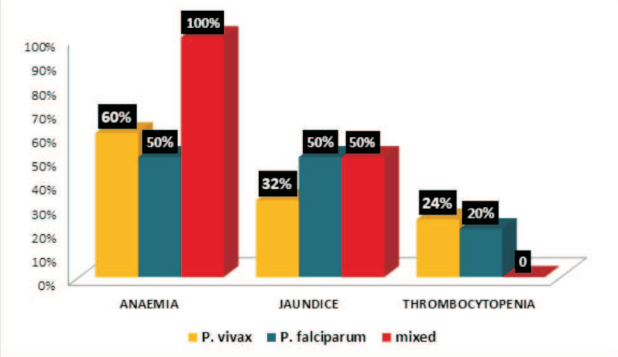

Fig. 1: *Difference in complications among vivax and falciparum patients: anaemia, jaundice, and thrombocytopenia.*

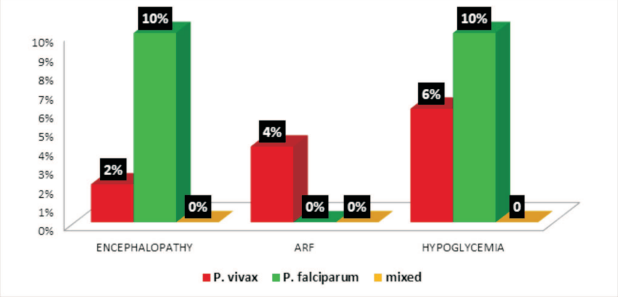

Fig. 2: *Difference in complications among vivax and falciparum patients: encephalopathy, acute kidney injury, and hypoglycaemia.*

Table I: Difference in various complications among vivax malaria and falciparum malaria.

S. No.	Complication	*P. vivax* (n = 50)	*P. falciparum* (n = 10)	Both (n = 4)	Total (n = 64)	
1.	Anaemia	30 (60%)	5 (50%)	4 (100%)	39 (60.9%)	$\chi^2 = 3.06$
2.	Jaundice	16 (32%)	5 (50%)	2 (50%)	23 (35.9%)	$\chi^2 = 0.582$
3.	Thrombocytopenia	12 (24%)	2 (20%)	2 (50%)	16 (25%)	$\chi^2 = 1.50$
4.	Encephalopathy	1 (2%)	1 (10%)	00 (0%)	2 (3.1%)	$\chi^2 = 1.93$
5.	Acute kidney injury	2 (4%)	00 (00%)	00 (0%)	2 (3.1%)	$\chi^2 = 0.513$
6.	Hypoglycaemia	3 (6%)	1 (10%)	00 (0%)	4 (6.3%)	$\chi^2 = 1.247$

Df = 2, chi square > 5.99 is significant.

Table II: Gender wise distribution of anaemia in malaria patients.

	Male No. (%)	Female No. (%)	Total No. (%)
Anaemic	10 (29.4%)	29 (96.7%)	39 (60.9%)
Non anaemic	24 (70.6%)	01 (3.3%)	25 (39.1%)
Total	34	30	64 (100%)

Discussion

Previously, *P. vivax* was considered the cause of Tertian malaria that rarely led to severe form of the disease.

Severe and complicated malaria is usually caused by *P. falciparum* but it has been increasingly observed that *P. vivax* malaria, which was otherwise considered to be benign malaria with low case fatality ratio, can also result in severe disease. Complications in severe malaria are either sequestration-related such as cerebral malaria, renal dysfunction, hepatic dysfunction and ARDS or non-sequestration related such as anaemia and thrombocytopenia[3].

Anaemia results from accelerated RBC removal by the spleen, obligatory RBC destruction by parasite schizogony, and ineffective erythropoiesis[2]. Anaemia was found to be a very important complication of malaria, whether *falciparum* or *vivax*. In our study anaemia was seen in 60% of *vivax* positive patients, while 50% of *falciparum* positive patients were anaemic, and it was 100% among patients of mixed infections. Non-sequestration complications like anaemia, thrombocytopenia, were also reported to occur more frequently in *P. vivax* infection by Kochar *et al*[3].

Thrombocytopenia is a well known complication of *P. falciparum* malaria but is also encountered in *P. vivax* malaria. This may be due to multiple factors which include increase in platelet destruction by platelet associated IgG antibody and its consumption[4,5]. In our study it was seen in 24% *P. vivax* patients and 20% patients of *P. falciparum*. Mixed infection had higher rate of approximately 50% of patients developed thrombocytopenia. In some studies thrombocytopenia was found in 12.5% patients[3].

Hepatic involvement has been well documented in *P. falciparum* malaria but also reported in *P. vivax* malaria. The possible explanation for hepatic involvement is direct injury to liver leading to malarial hepatitis[6,7,8]. In the present study jaundice was present in approximately 35.9% patients, in which *P. vivax* were 16 (32%), 5 were *P. falciparum* (50%) and 2 (50%) in patients with mixed infection. Similar findings were observed in one other study also[3].

Renal failure in malaria is caused by parasitised red blood cells leading to mechanical obstruction, microcirculatory disorders, disseminated intravascular coagulation, fluid loss, and hypoxic or immune mediated necrosis of renal tubules and glomeruli. These are the possible mechanisms that may be implicated in *vivax* infection[9-12]. In our study, acute kidney injury was seen in 4% of *P. vivax* positive patients while none among *falciparum* and mixed infections. So, renal complications were more reported in *vivax* patients.

Cerebral malaria is a very severe complication and one of the most common causes of mortality in malaria, though exact pathogenesis of cerebral malaria in *P. vivax* remains unknown. Few studies suggest that it might be due to sequestration and cytokine-mediated cerebral injuries[13,14]. However, increasing evidence has shown an increased risk of mortality and morbidity owing to *vivax* malaria. In our study, encephalopathy was seen in 3.1% of patients. Among *P. falciparum* positive, 10% develop encephalopathy, while only 2% of *P. vivax* positive patients develop encephalopathy.

Hypoglycaemia is a frequently encountered complication in *falciparum* malaria that is usually due to increased glucose use and impaired glucose production caused by the inhibition of gluconeogenesis[15]. In our study, 6% of *P. vivax* positive patients and 10% of *P. falciparum* positive patients developed hypoglycaemia. Though, it was more common in *falciparum* malaria but was an important complication in *vivax* malaria also.

In our study, none of the malaria patients developed ARDS and rupture of spleen, which is a significant cause of death. None of the admitted malaria patients died during course of treatment.

Conclusion

Though *falciparum* is well known for its complications, *vivax* malaria also causes severe complications. Acute kidney injury was found to be a significant complication in vivax malaria. The difference between the two was not significant but we should be aware of complications in *vivax* malaria too.

Limitation of study: The sample size was small in our study and it needs more comparison and study for further conclusion.

References

1. World Malaria Report 2018 (accessed on March 1, 2019). Available from: http://www.who.int/gho/malaria/en.
2. White NJ, Breman JC. Malaria. In Kasper DL, Fauci AS, Hauser SL *et al,* (eds). Harrison principles of internal Medicine 19th edition. New Yark: MC Graw HillL 2015; 1372-4.
3. Dhanpat KK, Ashish D, Sanjay KK *et al*. Severe Plasmodium vivax malaria: A report from severe cases from Bikaner in North Western India. *Am J Trap Med Hyg* 2009; 80 (2): 194-8.
4. Ohtaka M, Ohyashiki K, Iwabuchi H *et al*. A case of vivax malaria with thrombocytopenia suggesting immunological mechanisms. *Jap J Clin Hematol* 1993; 34 (4): 490.
5. Scott CS, VanZyl D, Ho E *et al*. Thrombocytopenia in patients with malaria: automated analysis of optical platelet counts and platelet clumps with the Cell Dyn CD4000 analyser. *J Clin Laboratory Haematol* 2002; 24 (5): 295-302.
6. Kochar DK, Singh P, Agarwal P *et al*. Malarial hepatitis. *J Assoc Phy Ind* 2003; 51: 1069-76.
7. Anand AC, Ramji C, Narula AS *et al*. Malarial hepatitis: a heterogeneous syndrome?. *Nat Med J Ind* 1991; 5 (2): 59-62.
8. Srivastava S, Ahmad S, Shirazi N *et al*. Retrospective analysis of vivax malaria patients presenting to tertiary referral centre of Uttarakhand. *Acta Tropica* 2011; 117 (2): 82-5.
9. Kochar DK, Agarwal P, Kochar SK *et al*. Hepatocyte dysfunction and

hepatic encephalopathy in Plasmodium falciparum malaria. *QJM* 2003; 96 (7): 505-12.

10. Premaratna R, Gunatilake AK, Desilva NR *et al*. Severe hepatic dysfunction associated with falciparum malaria. *South East Asian J Trop Med Pub Health* 2001; 32 (1): 70-2.
11. Patwari A, Aneja S, Berry AM *et al*. Hepatic dysfunction in childhood malaria. *Arch Dis Child* 1979; 54 (2): 134-39.
12. Singh R, Kumar S, Rana SK *et al*. A comparative study of clinical profiles of vivax and falciparum malaria in children at a tertiary care centre in Uttarakhand. *J Clin Diag Res* 2013; 7 (10): 2234-7.
13. Beg MA, Khan R, Baig SM *et al*. Cerebral involvement in benign tertian malaria. *Am J Trap Med Hyg* 2002; 67 (3): 230-32.
14. Kochar DK, Singh G, Tanwar P *et al*. Clinical features of children hospitalised with malaria – a study from Bikaner, northwest India. *Am J Trap Med Hyg* 2010; 83 (5): 981-9.
15. Thien HV, Kager PA, Sauerwein HP. Hypoglycaemia in Falciparum Malaria is fasting an unrecognised and insufficiently emphasized risk factor: Trends Parasital. *Trends Parasitol* 2006; 22 (9): 410-15.

Avas