

CO-INFECTION OF PLASMODIUM VIVAX AND FALCIPARUM MALARIA IN A TERTIARY CARE HOSPITAL IN BIHAR

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ABSTRACT

BACKGROUND

Malaria is probably one of the oldest diseases known to mankind that has had profound impact on our history. It continues to be a huge social, economic and health problem, particularly in the tropical countries. Studies on malaria due to co-existent *P. falciparum* and *P. vivax* infections are negligible in India. Therefore, this study was undertaken to find out the clinical profile, prognostic factors and outcome of mixed-species malaria and to compare it with *P. falciparum* malaria.

MATERIALS AND METHODS

A descriptive study was carried out on 100 patients of malaria admitted in Department of Medicine, Patna Medical College and Hospital, Patna, a tertiary care hospital from January 2016 to August 2017.

RESULTS

Out of 100 cases, 5 cases have both *falciparum* and *vivax* co-infection in infective positive cases. In 68 cases *P. falciparum* were positive and 27 were *P. vivax* positive.

CONCLUSION

Co-infection is not uncommon in the locality, where both species coexists. Co-infection can complicate with severe malaria. However, its incidence and severity is less than severe *falciparum* malaria. In mixed infection, *P. vivax* malaria has a protective effect against the severity of *falciparum* malaria.

KEYWORDS

Prevalence, Co-Infection, *P. falciparum*, *P. vivax*.

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BACKGROUND

Malaria was linked with poisonous vapours of swamps or stagnant water on the ground since time immemorial. This probable relationship was so firmly established that it gave the two most frequently used names to the disease malaria, later shortened to one word malaria (paludisme).¹ Malaria is a protozoal disease transmitted by the bite of infected anopheles mosquitoes. It is the most important of the parasitic diseases of humans with transmission in 107 countries containing 3 billion people and causing 1 - 3 million death each year. Malaria is a major cause of mortality and morbidity in the tropical and subtropical regions of the world. Developed countries are relatively free of malaria, but it remains well entrenched across the tropical world.²

The incidence of malaria worldwide is estimated to be 300 - 500 million clinical cases each year with about 90 percent of these occurring in Sub-Saharan Africa, and mostly caused by

P. falciparum.³ Of reported cases of malaria, India accounts for 77 percent of the regional total. Major endemic areas in India accounts for 77 percent of the regional total. Major endemic areas in India are in the North-Eastern states, Andhra Pradesh, Chhattisgarh, Gujarat, Jharkhand, Bihar, MP, Maharashtra, Rajasthan and Orissa.⁴

Five species of the genus Plasmodium cause nearly all malarial infections in humans. These are *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and in Southeast Asia the monkey malaria parasite *P. knowlesi*, which can be reliably identified only by molecular methods. Almost all deaths are caused by *falciparum* malaria. Clinical pictures, outcome, prognostic factors and changing clinical pattern of malaria due to individual species infection have been studied extensively.¹ In a geographical area when more than one species co-exist, sympatric combination of these infections in an individual cannot be ruled out. But the profile of malaria due to multiple species infection is considerably underestimated due to lack of studies.⁵

Human infection begins when a female anopheles mosquito inoculates plasmodium sporozoites from its salivary gland during a blood meal. These microscopic motile forms of the malarial parasite are carried rapidly via the bloodstream to the liver, where they invade hepatic parenchymal cells and begin a period of asexual reproduction. By this amplification process (known as intrahepatic or pre-erythrocytic schizogony or merogony), a single sporozoite eventually may produce from 10,000 to > 30,000 daughter merozoites. The

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swollen infected liver cell eventually bursts, discharging motile merozoites into the bloodstream. These merozoites then invade the red blood cells (RBCs) and multiply six- to twenty-fold every 48 - 72 h. When the parasites reach densities of 50/ L of blood (100 million parasites in the blood of an adult), the symptomatic stage of the infection begins. In *P. vivax* and *P. ovale* infections, a proportion of the intrahepatic forms do not divide immediately, but remain dormant for a period ranging from 3 weeks to a year or longer before reproduction begins. These dormant forms or hypnozoites are the cause of the relapses that characterise infection with these two species.⁶

Symptom of malaria include fever, shivering, arthralgia, vomiting, anaemia, haemolysis and jaundice, haemoglobinuria and convulsions. There may be a feeling of tingling in the skin, particularly with malaria caused by *P. falciparum*.⁷

The classical symptom of malaria is the cyclical occurrence of sudden coldness followed by rigor and then fever and sweating lasting for four to six hours, occurring every two days in *P. vivax* and *P. ovale* infections, while every three for *P. malariae*. *P. falciparum* can have recurrent fever every 36 - 48 hours or less pronounced and almost continuous fever. Splenomegaly, severe headache, cerebral ischaemia, hepatomegaly, hypoglycaemia and haemoglobinuria with renal failure may occur.⁸

Chronic malaria is seen in both *P. vivax* and *P. ovale*, but not in *P. falciparum*. Here, the disease can relapse months or years after exposure due to the presence of latent parasites in the liver. Describing a case of malaria as cured by observing the disappearance of parasites from the bloodstream can therefore be deceptive.⁹

If the patients with falciparum malaria have jaundice, vital organ complications should be looked for. Also, hyperpyrexia is no longer considered a sign of severity.¹⁰

The diagnosis of malaria is essentially made from clinical features and can be confirmed by demonstration of plasmodium by laboratory examination. Light microscopy demonstrates different stages of malaria parasite. The expected sensitivity that for the examination of the thick blood film procedure is about 50 parasites/ μ L of blood (assuming a total RBC count of 5×10^6 / μ L of blood), which is equivalent to 0.001% of RBC infected. Milne et al found that most routine diagnostic laboratories generally achieved a lower sensitivity of detection (average 0.01% RBC infected and 500 parasites/ μ L).¹¹

Warhurst and Williams reported that examination of thin blood films is only 1/10 as sensitive as examination of thick blood films for the quantification of malarial parasites, although morphological identification of the Plasmodium species present is much easier using thin films.

Certain fluorescent dyes have an affinity for the nucleic acid in the parasite nucleus and will attach to the nuclei. Two fluorochromes have frequently been used for this purpose, acridine orange (AO) and benzothiocarboxypurine (BCP). An alternative fluorochrome procedure using a solution of BCP reported sensitivity and specificity of >95% for *P.falciparum*.¹²

In this context, the knowledge about mixed species infection is important not only for control measures, but also for therapeutic options and futuristic vaccine programme. Therefore, we have undertaken this research to study the clinical pattern and outcome of mixed species malaria in adults and to compare it with Pf malaria in a tertiary care hospital.

MATERIALS AND METHODS

A descriptive study was carried out on 100 patients of malaria admitted in Department of Medicine, Patna Medical College and Hospital, Patna, a tertiary care hospital from January 2016 to August 2017. Cases were selected with complaint of untreated fever of short duration and/ or raised body temperature without any preexisting documented systemic illness with clinical features like fever-paroxysmal, remittent or intermittent, chills, anaemia, splenomegaly, hepatomegaly, headache, vomiting, drowsiness, altered behaviour, confusion, unarousable coma etc. Confirmation of diagnosis was made by demonstration of plasmodium in the peripheral blood by thin and thick blood film examination, by immunochromatographic test, Quantitative Buffy coat analysis for parasite and complete blood profile included platelet.

Statistical Analysis

After confirming the diagnosis of malaria by peripheral blood smear examination and/ or immunochromatography and/ or Buffy coat examination, 100 cases were studied under various aspects as described in material and methods. The outcome of the study was statistically analysed, tabulated and compared.

RESULTS

Out of these 100 patients 68 cases had Plasmodium falciparum infection, 27 had malaria from *P. vivax* and 5 patients had co-infection of falciparum and vivax infection. Out of 100 cases studied, 77 were male and 23 were female. The age of patient varied from 13 - 75 years. The maximum incidence of the disease was observed among patients in the age group from 21 years to 40 years in both sexes [Diagram 1].

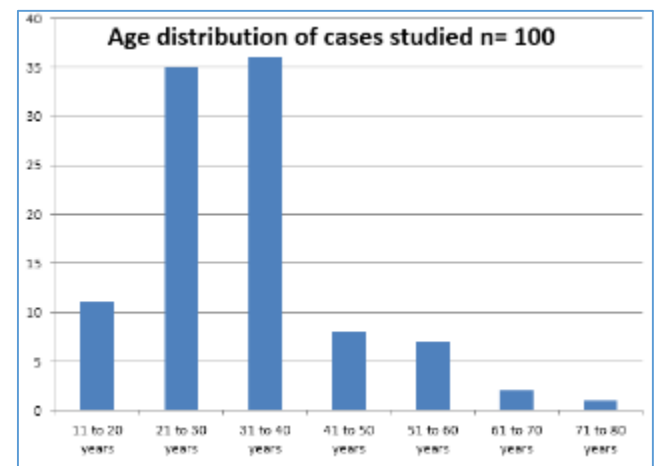


Diagram 1. Showing the Age Distribution of Cases Studied [n= 100]

Out of 100 cases 62 were diagnosed by light microscopy in peripheral blood smears, 95 cases were diagnosed by immunochromatography [Optimal IT]. Out of these 100 patients 68 cases had *Plasmodium falciparum* infection, 27 had malaria from *P. vivax* and 5 patients had combined *falciparum* and *vivax* infection [Diagram 2, Table 1].

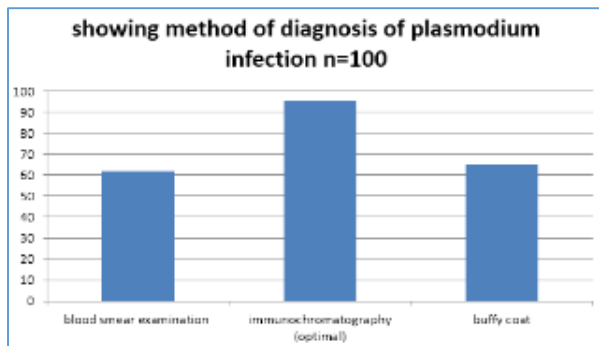


Diagram 2. Showing Diagnosis of Malaria Infection [n= 100]

Sl. No.	Plasmodium Species	No. of Cases
1.	<i>P. falciparum</i>	68
2.	<i>P. vivax</i>	27
3.	Combined (both falciparum and vivax)	5

Table 1. Showing No. of Cases of Different Types of Plasmodium Infection (n= 100)

DISCUSSION

The present study was carried out in 100 patients of malaria admitted in Department of Medicine, Anugrah Narayan Magadh Medical College and Hospital,¹ Gaya, a tertiary level hospital. The study period extended from January 2010 to August 2011. A total of 100 cases diagnosed as malaria and admitted in Medical Ward, Emergency and ICU were included for this study. 5 cases were diagnosed as having acute kidney injury as per RIFLE/ AKIN criteria in cases of malaria and comprising of different age groups ranging from 15 - 75 years and both sexes with male: female ratio of 3.0: 1. Besides fever (100%), headache (60%), vomiting (60%), convulsion (36%), unconsciousness (28%) and abnormal behaviour (33%) were other presenting complaints. Anaemia was present in 42%, jaundice was noted in 46%, hepatomegaly in 48% and splenomegaly in 86%, pulmonary oedema/ ARDS in 3%, diminished urine output in 24% and dark colour urine in 18%. Investigations revealed TLC > 12,000/ uL in 29%, haemoglobin < 10 gm% in 59% and severe anaemia (Hb% < 5 gm%) in 22%, serum bilirubin > 3 mg/ dL in 44% and SGPT >100 U/ L in 30%. Serum sodium was < 135 mEq/ L in 41% cases and serum potassium was > 5.5 mEq/ L in 22%. Blood sugar level was < 40 gm/ dL in 29%. Severe anaemia and jaundice were common manifestations. Extrarenal manifestation with associated mortality in all the cases of malaria (n= 100) was as follows: Severe anaemia had 18.18% mortality, hyperbilirubinaemia had 15.9% mortality, cerebral malaria had 25% mortality, pulmonary oedema had 100% mortality, hypoglycaemia had 31.03%, hyponatraemia had 21.95% mortality and hyperkalaemia had 22.7% mortality. Pulmonary oedema/ ARDS had highest mortality; hypoglycaemia is the next. Quantitative Buffy coat is a laboratory test to detect infection with malaria or other blood

parasites. 1. The blood is taken in a QBC capillary tube, which is coated with Acridine Orange [a fluorescent dye] and centrifuged; 2. The fluorescing parasite can then be observed under Ultraviolet light at the interface between RBC and Buffy coat.

CONCLUSION

In conclusion co-infection is not uncommon in the locality where both species coexist. Co-infection can complicate with severe malaria, but its incidence is significantly less suggesting a protective effect of *P. vivax* infection. It is important because if previous *P. vivax* infection does protect against severe *P. falciparum* infection, then control of vivax malaria may reduce the vivax-associated protection against severe falciparum infection enhancing increased incidence of severe falciparum malaria.

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