Original Research Article

# To Study the Hepatic and Renal Dysfunction in Various Species of Malaria in Mewat Region of Haryana

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## Abstract

**Introduction**: India contributes 80% of Southeast Asia malaria burden. The hepatic and renal injury in Malaria is well known. As our region has a high prevalence of Malaria so the purpose of our study is to evaluate the hepatic and renal insult in all species of Plasmodium prevalent in the region.**Materials and Methods**: A Case control observational study was done on 90 malaria positive cases in SHKM Medical College and hospital Nuh, Haryana from the month of July 2017 to Dec. 2017. Malaria was confirmed by both Rapid kit method and by Peripheral blood smear. Blood and urine were analyzed for liver function tests and renal dysfunction. A case control observational study analysed using SPSS software.**Results**: Out of all 90 malaria positive cases, 38 % were P. falciparum, 51 % were P. vivax and 11 % were mixed infection. After doing liver function test, it was determined that 50% of these were of P. vivax and 42% were of P. falciparum. Similarly, with kidney function test, raised creatinine level and urine microprotein level were seen in 42% P. falciparum and 49% P. vivax.**Conclusion**: With changing spectrum different grades of biochemical and hematological changes generally found to be more severe with P. falciparum, are now frequently seen with P. vivax. P. vivax can no more be considered benign. P. vivax is now considered to be lethal due to dormant stage hypnozoites leading to relapse and greater transmission even at low parasite densities.

**Keywords:** Malaria, Plasmodium, Liver Function Test, Kidney Function Test.



## Introduction

Malaria has long been recognized as one of the most important parasitic disease of humans that primarily affects tropical countries worldwide, making it a major international public health problem. According to World Malaria Report 2019, an estimated 228 million cases of malaria occurred worldwide during 2018 and nineteen countries in sub-Saharan Africa and India carried almost 85% of the global malaria burden.[1] According to one study in South-East Asian region, out of approx. 1314 million population at risk for *P. falciparum* malaria, there are 119 million cases (34%) positive for *P. falciparum* malaria; out of 1347 million population at risk for *P. vivax* malaria, there are 90-248 million (63%) positive cases and 156-472 million cases (18%) positive for mixed infection, India alone contributed 76% of total cases.[2]

Malaria is transmitted via the bite of a female anopheles mosquito, which occurs mainly between dusk and dawn. Other comparatively rare mechanisms for transmission include congenitally-acquired disease, blood transfusion, sharing of contaminated needles, and organ transplantation.[3]

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It is a vector borne parasitic disease caused by the genus *Plasmodium*. Four species of *Plasmodium* mainly responsible for causing malaria in human are *Plasmodium falciparum*, *P. vivax*, *P. malariae* and *P. ovale*. Certain times, several simian species can infect human beings, either naturally or on accidental exposure, such as *P. knowlesi*, *P. brasilianum*, *P. cynomolgibastianelli*, *P. schwetzi* and *P. inui*.[4]

*P. falciparum* malaria generally causes more severe disease, mortality and morbidity, so intensive measures have been implemented against it. *P. vivax* malaria has been neglected and is considered as "Benign".[5] But recently complications caused by *P. vivax* have become more prevalent. Early recognition of clinical symptoms predictive of the onset of complications would allow prompt treatment and supportive care to prevent progression to death.[6]

The presenting symptoms of malaria are nonspecific and include fever, tachycardia, tachypnea, chills, malaise, fatigue, diaphoresis, headache, cough, anorexia, nausea, vomiting, abdominal pain, diarrhea, arthralgia, and myalgia. Physical findings may include mild pallor, petechiae, jaundice, hepatomegaly and/or spleenomegaly.[7,8]

As the malaria infection progresses some clinical features indicate the establishment of serious illness and are danger signs for a complicated phase of the disease.[6] The commonest complications associated are cerebral malaria, severe haemolytic anaemia, pulmonary oedema, acute respiratory distress syndrome (ARDS), thrombocytopenia, disseminated intravascular coagulation, shock, renal involvement, kidney failure and hepatic dysfunction.[9,10,11]

As Malaria is highly prevalent in our region, this study is done to evaluate the effects of malaria infection on liver and kidney, with respect to all species of *Plasmodium* prevalent in the region.

**Aims**

1. To study the hepatic and renal injury in all cases of Malaria and to add on the knowledge of clinical profile of different species of *Plasmodium*.
2. Early diagnosis of acute renal failure and intervention in subjects who have hepatic dysfunction in malaria, which can save many lives.

**Subjects and Methods**

A Case control, prospective, observational study was done on 90 malaria positive cases in SHKM Medical College and hospital Nuh, Haryana from the month of July 2017 to Dec. 2017.

**Inclusion Criteria**

Only those patients who were having fever for more than three days and smear positive were included in the study.

**Exclusion Criteria**

(1) Patients presented with fever (smear negative for *Plasmodium*) but treated empirically for malaria.

(2) Patients presented with clinical features mimicking malaria like dengue fever, sepsis, meningitis were excluded from this study.

The diagnosis and confirmation of species of *P. falciparum* and *P. vivax* malaria were established by thick and thin film of peripheral blood smear examination and Rapid Diagnostic Tests. The RDTs were based on detection of specific *Plasmodium* spp. lactate dehydrogenase and histidine-rich protein

The peripheral blood films were prepared from prick of finger, stained by conventional Giemsa stain seen under oil immersion (100×) taking care to examine particular upper and lower margins and tail end of the film and a minimum of 100 fields were examined before declaring the slides negative for *Plasmodium*.[3]

The blood was analysed for liver function tests by measuring AST, ALT, ALP and Total Bilirubin. And serum creatinine and urine microprotein was done to assess the renal dysfunction. Blood and urine test were done on Roche biochemistry analyzer.

Data was analyzed by SPSS for data analysis.

**Results**

Total 90 patients with confirmed malaria cases were included in this study. Out of these 55 patients were male (61%) and 35 were female (39%). Thus, Male to female ratio for malaria infection was 1.6:1.

About 34 patients (38%) were infected by *P. falciparum*, 46 patients (51%) by *P. vivax* and 10 patients (11%) were infected by both (mixed infection).

**Liver Function Test:** 66(73%), 72(80%), 48(53%) and 68 (75%) malaria positive patients were found to be having higher level ($p>0.05$) of AST, ALT, ALP and total bilirubin respectively than malaria free individuals. 50% of these were of *P. vivax* and 42% were of *P. falciparum*.

**Kidney Function Test**: 51 (57.79%) of patients had creatinine level above normal range of 1.2 mg/dl. In 56(62%) malaria positive patients, random urine microprotein level was also higher than the normal value of 10mg/dl, which was also significant. Of this 42% were *P. falciparum* and 49% were *P. vivax*.

**Table 1: Sex wise distribution of Malaria patients**

| S. No. | Sex | No of Patients (Percentage) |
|---|---|---|
| 1 | Male | 55 (61%) |
| 2 | Female | 35 (39%) |
| Total | | 90 |

**Table 2: Species wise distribution of Malaria patients**

| S. No. | Plasmodium species | Number of cases (Percentage) |
|---|---|---|
| 1 | *P. falciparum* | 34 (38%) |
| 2 | *P. vivax* | 46 (51%) |
| 3 | Mixed infection | 10 (11%) |
| Total | | 90 |

**Table 3: Comparison of liver function tests for subtypes of Malaria**

| Liver Function Test | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Parameter | | | | | | | |
| Species | T. Bilirubin | | AST | | ALT | | ALP | |
| | < 1 mg/dl | > 1 mg/dl | < 40 IU | > 40 IU | < 40 IU | > 40 IU | < 120 IU | > 120 IU |
| *P. falciparum* (N=34) | 6 | 28 | 12 | 22 | 5 | 29 | 16 | 18 |
| *P. vivax* (N=46) | 14 | 32 | 11 | 35 | 9 | 37 | 18 | 28 |
| Mixed parasites (N=10) | 2 | 8 | 1 | 9 | 4 | 6 | 8 | 2 |
| Total | 22 | 68 | 24 | 66 | 18 | 72 | 42 | 48 |

**Table 4: Comparison of kidney function tests for subtypes of Malaria**

| Kidney Function Test | | | | |
|---|---|---|---|---|
| | Parameter | | | |
| Species | Creatinine | | Urine microprotein | |
| | < 1.2 mg/dl | > 1.2 mg/dl | < 10 mg/dl | > 10 mg/dl |
| *P. falciparum* (N=34) | 14 | 20 | 11 | 24 |
| *P. vivax* (N=46) | 21 | 25 | 17 | 28 |
| Mixed parasites (N=10) | 4 | 6 | 6 | 4 |
| Total | 39 | 51 | 34 | 56 |

**Discussion**

Malaria is responsible for large number of morbidity and mortality in our country. Out of the four well known species, most common species of *Plasmodium* found in India are *Plasmodium falciparum* and *Plasmodium vivax*. Many complications may arise following *P. falciparum* infections. Although initially considered benign, *P. vivax* is found to be associated with hepatic and renal dysfunction in similar manner as *P. falciparum*. To compare the two species infection, a study was conducted in Nuh, Haryana from June 2017 to September 2017 and total 90 patients with confirmed malaria diagnosis were included in this study.

In our study, the ratio of male (61%) to female (39%) patients was 1.6:1. This was in accordance with the study by Rathod Chirag et al. In their study, male to female ratio was 1.8:1 in *P. falciparum* malaria and 0.8:1 in *P. vivax* malaria ($p <0.01$).[3]Similarly in another study, out of the 100 patients, 65 patients were males and 35 were females.[12] Similar findings were found in other studies also.[6,13]In this study, 34 patients (38%) were infected by *P. falciparum*, 46 patients (51%) by *P. vivax* and 10 patients (11%)

were infected by both, i.e. the infection by *P. vivax* was more common than *P. falciparum*. In India, about 70% of the infections are reported to be due to *P. vivax*, 25-30% due to *P. falciparum* and 4-8% due to mixed infection.[12,14] In another study, among the three groups of vivax, falciparum and mixed malaria, the proportion of infection was 81.5%, 3.4%, and 15.1% respectively.[13] In a similar study by Goyal et al. the cases consisted of 47 *P. vivax* and 32 *P. falciparum* infection.[15]Other studies showed the more cases of *P. falciparum* infection than *P. vivax*. In a study, of the 781 slide positive patients, 443(57%) were *P. falciparum* cases, 327 (42%) were *P. vivax* cases and 11(2%) were mixed infection, as shown in table1.[3] Similarly in another study, 64% of the total cases were of *P. falciparum*, 24% cases were due to *P. falciparum*, and 12% were due to mixed infection with *P. falciparum* and *P. falciparum*.[12] In a study at Colombo, *P. falciparum* infection was diagnosed in 419 (67.9%), *P. vivax* in 187 (30.2%), and mixed infection by these species in 14 (2.3%).[6]

**Association with Hepatic Dysfunction**

In our study, hepatic dysfunction was found to be associated more with *P. vivax* infection then *P. falciparum*. 50% of cases were of *P. vivax* and 42% were of *P. falciparum*. Total bilirubin was found to be raised in total 68 (75%) patients out of whom 28 (41%) were infected with *P. falciparum*, 32 (47%) with *P. vivax* and 8 (12%) with mixed infections. Similarly, 66 (73%) patients showed raised levels of AST, 72 (80%) patients raised levels of ALT and 48 (53%) patients showed raised levels of ALP enzymes, in relation to malaria free persons, respectively.Similar findings were found in various other studies. Like in a study done in Vadodra, 2011, altered liver function test or malarial hepatopathy (increased S. bilirubin, SGPT) was seen in 237 cases (51%) of *P. falciparum* and 215 cases (65%) of *P. vivax* patients. Whereas raised indirect bilirubin was seen in 58 cases (13.09%) of *P. falciparum* and 23 cases (7.03%) of *P. vivax* malaria.[3]Similarly, hepatic dysfunction was found in 57.3%, 39.2% and 74.7% – vivax, falciparum and mixed malaria infections, respectively, in a study by Akshatha et al in 2017.[13]

In a similar study, raised liver enzyme and jaundice were present in 10.6% and 6.3% of *P. vivax* cases while the same were present in 6.2% and 9.3% cases of *P. falciparum*.[15]

**Association with Renal Dysfunction**

In our study, renal impairment was determined with measuring, serum creatinine level and urine microprotein level. Out of all the patients showing renal dysfunction, 42% were *P. falciparum* and 49% were *P. vivax*. Among them, 51 (57.79%) of patients had creatinine level above normal range of 1.2 mg/dl, where 20 (58.8%) were from 34 *P. falciparum* infection, 25(54%) from 46 *P. vivax* infection and 6 (60%) among 10 mixed infection. In malaria positive patients, random urine microprotein level was higher in 70.6% (24 out of 34) *P. falciparum* infection, 60.9% (28 out of 46) *P. vivax* infection and 40% (4 out of 10) mixed infection. This suggest that although in total malaria positive patients, cases of *P. vivax* infected patients showing renal dysfunction was higher but on individual level, chances of developing renal dysfunction were more common in *P. falciparum* infection. In another study, acute renal failure was present in 30% of the cases of malaria who were admitted in the hospital. 11 (36.7%) of the cases having renal failure were due to *P. falciparum*, 13 (43.3%) were due to *P. vivax* and 6 (20%) cases had mixed infection with *P. falciparum* and *P. vivax*. Their study further reveals that out of all 24 (100%) cases of *P. falciparum* 11 (46%) and out of 12 (100%) of mixed PV and PF 6 (50%) had renal dysfunction in comparison to 13 (20%) out of 64 in *P. vivax*. These findings were statistically significant (p - 0.018) and were similar to our study.[14]Similarly in a study, renal failure was encountered in 2.1% and 3.1% of *P. vivax* and *P. falciparum* cases in our study, respectively.[15] In a study, renal dysfunction was seen in 49 cases (11.06%) of *P. falciparum* and 38 cases (11.6%) of *P. vivax* malaria, respectively.[3] These results were also similar to study done by Das in 2008.[16]

**Key Message**

Previously, P. falciparum was supposed to cause complications in Malaria, but now studies suggest that spectrum of complications by P. vivax infection is changing and is causing hepatic and renal impairments in patients. The knowledge is very important for early diagnosis and treatment of malaria to avoid complications.

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