Research Article

Clinicopathological profile of malaria in Bareilly

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ABSTRACT

Background: Malaria is the major cause of infectious disease death in India. *Plasmodium vivax* (PV) is the most common cause of malaria among humans affecting about 25 billion population worldwide. India is having 80% of malaria cases among South East Asia region. India being the country having different geographical regions and climate, the pattern of malaria vary with places. **Objectives:** This study was done to study the clinical features, diagnosis, laboratory investigations, outcome, and complications of malaria in a tertiary care hospital of Bareilly. **Materials and Methods:** A prospective analysis of adult patients suffering from malaria was carried out during the year 2014-2015. Diagnosis of the patients was done on clinical features, peripheral smear examination, and rapid diagnostic test. The parasitic count was done from peripheral blood smear. The clinical features, laboratory investigations, treatment, and outcome were studied. The response to treatment was determined on the basis of improvement of clinical features and repeated peripheral blood smear examinations. **Results:** Out of the 126 patients, 71 (56.34%) were males and 55 (43.65%) were females in the age group of 15-70 years. Fever was universal presentation ($P < 0.001$). 47.6% of the patients complained of headache, 29.36% had vomiting. Jaundice was observed in 20.63% patients. Anemia was present 53.17%. All above results were statistically significant. 15.87% presented with loss of sleep, 7.93% as acute abdomen, 4.76% as convulsion, and 3.96% as bleeding as a result of thrombocytopenia (statistically non-significant). Among 126 malaria cases, 62 (49.2%) were with PV, 36 (28.57%) with *Plasmodium falciparum*, and 18 (14.28%) had mixed infection. 10 were smear negative patients, and they received empirical treatment on the basis of sign and symptoms of malaria. **Conclusion:** Majority of hospitalized patients were *vivax* positive. Complicated malaria was seen with *Falciparum* infection. Clinical symptomatology without blood smear positivity can be the basis of starting treatment. Epidemiological survey for drug resistance should be considered while planning an antimalarial strategy.

KEY WORDS: *Plasmodium Vivax*; *Plasmodium Falciparum*; Cerebral Malaria

INTRODUCTION

Malaria is the most serious vector-borne disease and it is the major cause of death worldwide. The worldwide prevalence of malaria is estimated to be approximately 300-500 million clinical cases each year and is endemic in 101 countries. Human malaria is caused primarily by four different species of *Plasmodium*, namely; *Plasmodium falciparum* (PF), *Plasmodium vivax* (PV), *Plasmodium malariae* (PM), and *Plasmodium ovale*. Clinical features and clinical pattern of malaria due to individual species infection have been studied extensively.[1] When more species coexist, combination of these infections in an individual can exist.[2] The 60-65% of the infections in India are due to PV and 35% due to PF. There has been a decline in the total number of cases in India, but *Falciparum* had a significant increase. The

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mortality in malaria is due to PF.[3] Malaria is a febrile illness characterized by fever and related symptoms. It is very important to remember that malaria is not a simple disease of fever, chills and rigors. In fact, in endemic area, it can present with varied and dramatic manifestations that malaria may have to be considered as a differential diagnosis for almost all the clinical problems. The awareness of atypical presentation is important to detect cases of malaria in endemic areas. Atypical features are more common in *Falciparum* malaria, early infection, extremes of age, immune-compromised (extremes of age, malnourished, acquired immunodeficiency syndrome, tuberculosis, cancers, and on immunosuppressive therapy), patients on chemoprophylaxis for malaria, patients who have had recurrent attacks of malaria, patients with end-stage organ failure and pregnancy. Malaria once classified as disease of villages now diversified under the pressure of developments into various ecotypes as forest malaria, urban malaria, rural malaria, industrial malaria, border malaria, and migration malaria. India being a vast country with different geographical regions, the pattern of the disease may vary from one place to the other. Various studies were available as per different regional studies across India regarding malaria, but no study was available for Bareilly region. This study was undertaken to study the clinical features and complications in a tertiary care hospital in Bareilly district of Uttar Pradesh (India).

MATERIALS AND METHODS

This prospective study of malaria was conducted at Rohilkhand Medical College and Hospital Bareilly (Uttar Pradesh, India) from January 2014 to March 2015. Males and females suffering from malaria of 15 to 70 years of age group admitted in medicine ward were included in the study after proper consent from the patient's side and approval from the institutional ethical committee. The total 160 patients were included in the study, out of which 34 left because of incomplete follow-up. Hence, the total effective number of malaria cases in the study were 126. Out of which, 71 were males and 55 were females. The diagnosis of the malaria was done by clinical features and blood peripheral smear. The diagnosis of *Plasmodium* species infection was made by either with detection of gametocyte of PF and PV from Giemsa-stained peripheral blood smear or rapid diagnostic test (RDT). The parasitic count was done from the peripheral blood smear. Parasite counts were expressed as numbers of asexual parasites per microliter of blood and were calculated from the numbers of parasitized cells per 200 leukocytes in a thick film stained with Giemsa stain, i.e., Number of parasites X total leukocyte count/200. Gametocyte counts are made from thick films. On admission, clinical work up has been done in accordance with the pro forma designed for this study. It includes history of previous attack of malaria, slide positive report, and clinical examination. The laboratory investigations done were complete blood count, blood picture, blood glucose, kidney function test, liver function test, glucose-6-phosphate dehydrogenase, serum sodium, and potassium. Severe malaria was diagnosed according to the guidelines of World Health Organization (WHO).[4] The statistical analysis was performed by Chi-square tests the treatment response was noted clinically and by repeated blood smear. It has been observed that if the features of malaria and slide positivity reappear within 2 weeks of treatment, the condition can be called recrudescence due to resistance. If the features recur between 2 and 4 weeks, it may be due to either relapse or recrudescence. If the features occur after 4 weeks, it is most probably due to relapse.

RESULTS

Out of the 126patients, 71 (56.34%) were males and 55 (43.65%) were females in the age group of 15-70 years. Fever was universal presentation ($P < 0.001$). The duration of fever was around 2-7 days. 47.6% of the patients complained of headache, 29.36% had vomiting. Jaundice was observed in 20.63% patients. Anemia was present 53.17%. All the above results were statistically significant. 15.87% presented with loss of sleep, 7.93% as acute abdomen, 4.76% as convulsion, and 3.96% as bleeding as a result of thrombocytopenia (statistically nonsignificant) (Table 1). Among 126 malaria cases, 62 (49.2%) were with PV, 36 (28.57%) with PF and 18 (14.28%) had mixed infection. 10 were smear negative patients, and they received empirical treatment on the basis of sign and symptoms of malaria (Table 2). Distribution of species is not statistically significant ($P = 1$). The complications of malaria were seen in 12 patients. The complications were cerebral malaria, hepatic failure, renal failure, bleeding, and thrombocytopenia (Table 3). The incidence of complications was statistically not significant. There was no death reported in the present study.

All the patients responded to treatment. Patients with chloroquine resistance/*Falciparum* malaria/complicated

Table 1: Distribution of the patients according to signs and symptoms

Sign and symptoms	Patients *n* (%)
Fever	126 (100)
Anemia	67 (53.17)
Head ache	60 (51.6)
Vomiting	37 (31.6)
Jaundice	26 (20.7)
Loss of sleep	20 (15.87)
Fainting attacks	12 (9.52)
Acute abdomen	10 (7.93)
Convulsion	6 (4.76)
Bleeding	5 (3.96)
Thrombocytopenia	5 (3.96)

Table 2: Distribution of the patients according to identification of malaria species on peripheral smear

Species	*n* (%)	Severe malaria
PV	62 (49.2)	0
PF	36 (28.57)	9
Mixed	18 (14.28)	3
Smear negative	10 (7.96)	0

PV: *Plasmodium vivax*, PF: *Palsmodium falciparum*

Table 3: Distribution of the patients according to complications of malaria

Complications	Patients *n* (%)
Cerebral malaria	6 (1.9)
Hepatic failure	5 (1.9)
Renal failure	8 (9.3)
Bleeding	5 (1.9)
Thrombocytopenia	5 (3.7)

malaria received artesunate injections. Chloroquine resistance was seen in 11 patients of *Vivax* group as per the WHO guidelines for extended field tests.[5] Chloroquine resistance has been defined as the ability of the malarial parasite to survive and/or multiply despite administration and absorption of the drug given in doses equal or higher than usually recommended but within the tolerance of the subject.[6]

DISCUSSION

The considerable morbidity and mortality in malaria are mainly because of multiorgan involvement, delayed diagnosis, atypical presentation, inadequate treatment, and drug resistance.[7,8] Thus, one should be alert to the symptoms and signs that may progress to the life-threatening disease of malaria. Consideration of atypical presentation is important in endemic areas for search for parasite in the peripheral blood film in all the patients. The clinical suspicion can be the basis of starting the treatment of malaria whether the patient is diagnosed on peripheral blood smear or not. In the present study, fever was universal presentation ($P < 0.001$). The duration of fever was around 2-7 days. 47.6% of the patients complained of headache, 29.36% had vomiting. Jaundice was observed in 20.63% patients. Anemia was present in 53.17%. All the above results were statistically significant. 15.87% presented with loss of sleep, 7.93% as acute abdomen, 4.76% as convulsion, and 3.96% as bleeding as a result of thrombocytopenia (statistically nonsignificant) (Table 1). Among 126 malaria cases, 62 (49.2%) were with PV, 36 (28.57%) with PF, and 18 (14.28%) had mixed infection. 10 were smear negative patients, and they received empirical treatment on the basis of sign and symptoms. They were responded to treatment, and thus further complication of disease was prevented.

Another study from India has described the presentation of *Falciparum* malaria comprising convulsion in 28.55%, abdominal pain in 5.7%, hemiplegia in 2.8%, generalized weakness and palpitation in 5.5% of cases.[9] In the present study, the complicated malaria was seen in 12 patients. Nine were *Falciparum* and three were mixed (both *Vivax* and *Falciparum*) infection. The cause of complication in *Falciparum* malaria is the sequestrations of erythrocytes containing parasites in the vascular beds of internal organs.[10] The present study showed that mixed species malaria was found in 18 (14.2%). Population-based studies reported that mixed infection constituted <2% of total malaria infection.[6] Clinical studies from Thailand concluded that 30% of patients with PF malaria had suffered from symptomatic PV malaria.[11] In a population study where all the 4 species were present, the prevalence of double species infection diagnosed with polymerase chain reaction (PCR) was as high as 36.4% and triple infection was 23.7%.[12] Since PCR method is costly and not available widely, RDT in addition to slide test for the diagnosis of mixed malaria was used in present study. The available studies have used only the slide test for the diagnosis of malaria.[13,14] The present study had 14.2% cases of mixed infection which is in agreement with other another study (12.7%).[15] The severe malaria was higher in *Falciparum* than mixed. This is the beneficial effect of mixed species infection. The coincident infection of PF and PV reduces the risk of severe malaria due to PF by 4 fold.[2,16] This is protective potential of PV against PF, and thus PV is considered as the best available *Falciparum* malaria vaccine. In mixed PM and PF malaria infection, PM protects the severity of *Falciparum* malaria.[11] A study from Gujarat state (India) PV was found to account for 69% of all malaria cases and PF for the other 31%. Infection by PV and PF (63.13%) was commonest age group of 16-40 years.[17] Anemia is an important cause for high morbidity and mortality in malaria. Pathogenesis of anemia in malaria is multifactorial. A complex chain of pathological processes involving parasite-mediated red blood cell (RBC) destruction, marrow suppression and accelerated removal of RBCs. A study from Orissa, 86.7% had anemia.[18] The present study demonstrated anemia in 53.17% patients. 5 patients had decreased platelet count. Thrombocytopenia is a common complication in *Falciparum* malaria with spontaneous recovery on treatment. The cause of thrombocytopenia is disseminated intravascular coagulation (DIC) or removal of platelets by the reticuloendothelial system.[19] The present study showed hepatic failure in 5 patients. Hepatic failure in *Falciparum* malaria results from intravascular hemolysis of parasitized RBCs, hepatic dysfunction, and an element of microangiopathic hemolysis due to DIC.[20] Cerebral malaria is worst complication of *Falciparum* malaria. Cerebral malaria was seen in 6 patients, and all were *Falciparum* positive. The altered sensorium with fever may sudden or gradual usually associated with seizure episode. Chloroquine is drug of choice in PV malaria because of its low cost, tolerance, suitability for pregnant women and young children and easy availability. PV resistance to

chloroquine is a community problem for the treatment of malaria. The chloroquine resistance was seen in 11 patients. The chloroquine resistance, especially in *Falciparum* malaria, is due to the use of the drug in suboptimal doses or by prophylactic use of the drug in people living in the endemic zone or genetic mutation of the parasite. Thus, the suboptimal dose and prophylactic use in the endemic zone is not recommended except in travellers from the nonendemic to the endemic zone. The early detection of chloroquine resistance and management are essential to cure the disease and prevent the transmission of chloroquine resistance in the community. Drugs for chloroquine-resistant malaria are quinine, sulfadoxine-pyrimethamine combination, mefloquine, artesunate and its derivatives, halfantrine and certain antibiotics.[21]

This is a hospital based study representing only tip of iceberg of the patients of malaria in community. This study was done in admitted patients in the tertiary care center. Follow-up was poor as 34 patients left the study. Exact burden of malaria could not be assessed by this study. Further epidemiological study involving door to door surveillance and participation of primary caregiver is needed.

CONCLUSION

Malaria should be suspected in all cases of fever of 2-7 days duration. The majority of hospitalized patients were *Vivax* positive. Fever was the most common presentation. Complicated malaria was seen with *Falciparum* infection. Treatment of malaria can be started on the basis of clinical suspicion to avoid complication if laboratory report is inconclusive. Drug resistance should be considered while planning an antimalarial program for community.

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