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Original Research Article

Analysis of clinical profile and prescription pattern of malaria in a tertiary care hospital in Karnataka, India

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ABSTRACT

Background: Malaria is one of the leading causes of morbidity and mortality in developing countries like India. Plasmodium falciparum and Plasmodium *vivax* are the commonest species implicated for an increased incidence of malaria in India. The pattern of disease, signs, and symptoms vary from place to place, region to region due to demographic variations. The current study was undertaken to study the differences in the clinical profile of malaria, particularly signs and symptoms, complications and response to treatment in malaria.
Methods: A retrospective, single center, surveillance study was carried out at a tertiary health care center in Mangalore. All patients aged above 18 years diagnosed as malaria by peripheral smear method and rapid diagnostic tests were included in the study. The clinical features, complications, and response to treatment were noted.
Results: Fifty eight patients diagnosed as malaria were included in the study. Compared to other studies and nationwide incidences, here *P. vivax* emerged as the leading cause of malaria. All patients presented with fever varying from 3-20 days. About 30 patients complained of headache and 21 patients presented with malaise. In about 6 patient's complications were seen. Majority of patients received artemisinin derivatives followed by chloroquine for treatment of malaria
Conclusions: Previous thinking that complications are only seen with *P. falciparum* has to be changed. Now many complications, mild as well as severe type are seen in *P. vivax* malaria. Drug resistance is another global problem which needs to be tackled wisely by systematic usage of antimalarials.

Keywords: Artemisinin, cerebral malaria, Malaria, *P. vivax*

INTRODUCTION

Malaria is a highly endemic protozoal disease in India caused by Plasmodium species largely by *P. vivax* and *P. falciparum* and transmitted by the bite of female anopheles mosquito.[1] According to the World Malaria Report 2015, 14% (181.3 m) of India's population lives in high transmission (>1 case per 1000 population) areas, 77% (997.4m) live in low transmission (0-1 case per 1000 population) areas and 9% (116.6 m) live in malaria-free (0 cases) areas.[2] According to the latest reports by Indian National Vector Borne and Disease Control Programme in 2014, 1.1 million malaria cases have been recorded and 561 deaths.[3] The incidence of malaria in India accounted for 58% of cases in the South East Asia Region of WHO.[4]

Malaria continues to be a major public health hazard and malaria caused by *P. falciparum* is the main culprit for almost all severe cases of malaria and deaths due to malaria in India. P. vivax is the next major species causing mainly a febrile illness and rarely leads to severe disease. In 2012, *P. falciparum* accounted for more than 50% cases and killed 519 people in India with annual parasite index (API) of 0.884.[5] Recently due to effective interventional programs, there was a dramatic reduction in the number of cases.

The need of the hour is to define, the correct prescribing pattern and equally important is to identify irrational prescribing and to rectify it before drug resistance becomes a major problem. A medical audit helps in improving the standards of medical care by identifying all these major problems.[6]

The emergence of complications like thrombocytopenia with malaria due to P. vivax has changed the dimensions in the treatment of malaria. Drug resistance in the treatment of malaria is due to ineffective and inappropriate prescribing practices. Under dosing or overdosing of anti-malarial drugs leads to an increase in drug resistance and leads to treatment failure and an increase in morbidity and mortality from malaria.[6-8]

Increase in the presentation of malaria cases with atypical symptoms further leads to delay in diagnosis, treatment of malaria which in turn leads to increase in morbidity and mortality and also increase in the number of cases of complicated malaria. The current study was conducted to study the clinical profile and complications seen in malaria.

METHODS

The study was carried out after obtaining institutional ethics committee approval (IEC/SIMS&RC/44/2014).

Study design

This was a hospital-based, single-center retrospective surveillance study analysing the records of patients admitted with the diagnosis of Malaria and patients attended the OPD of medicine from Jan 2015 to June 2015 in a tertiary care center.

The information relating to patient age, gender, Mode of diagnosis, Lab reports and prescribing pattern of anti-malarial drugs were extracted and analyzed.

Study criteria

Patient of either sex aged above 18 years who were diagnosed as malaria either by rapid diagnostic tests (RDT) or peripheral smear test was included in the study. Patients presenting with a history of fever but their peripheral smear and rapid diagnostic test negative, still empirically treated with antimalarials were excluded from the study. patients aged below 18 years were also excluded from the study. Patients presented with symptoms mimicking malaria-like sepsis, dengue fever, leptospirosis were excluded.

Source of data

- Case sheets of inpatients diagnosed and admitted with malaria
- OPD cards of patients with a probable diagnosis of malaria visiting the department of medicine in a tertiary care hospital, Surathkal, Mangalore
- Lab reports of malaria patients

Statistical analysis of this study Percentage analysis was done using Microsoft Excel.

RESULTS

On the basis of our inclusion and exclusion criteria, 58 patients who attended our OP and IP department and diagnosed with malaria were considered for our study.

Out of 58 patients taken, 41 were males and 17 were females. Many of the patients were between the age group of 30-49 years (Table 1).

Table 1: Demographic details of patients.

Characteristics	N=58
Gender	
Male	41
Female	17
Geographical distribution	
Rural	48
Urban	10
Age group (in years)	
18-30	10
31-50	25
51-65	11
65 and above	12

Among 58 patients, 8 were infected from P. falciparum, 38 from *P. vivax* and 12 had mixed infection (Table 2). All 58 patients presented with a history of fever which was statistically highly significant. Headache and malaise were seen in 30 and 21 patients respectively. Anemia was a major sign in 18 patients and around 15 patients complained of vomiting. Jaundice and seizure were rarely seen in 5 and 2 patients respectively (Table 3).

Table 2: Details of microbiological diagnosis of patients.

Species	No of patients (N=58)
P. vivax	28
P. falciparum	14
Mixed infection	16

Out of 58 patients, 6 patients had complications during the time course of treatment. Out of 6 patients who had complications 5 were infected with *P. falciparum* and 1 with *P. vivax*. Out of 6 patients, 2 had cerebral malaria, 2 had liver dysfunction, 1 had renal failure and 1 had thrombocytopenia.

Table 3: Signs and symptoms of malaria patients in this study.

Signs and Symptoms	No. of patients
Fever	58
Vomiting	15
Malaise	21
Anemia	18
Headache	30
Gastritis	3
Jaundice	5
Diarrhoea	3
Seizure	2

Table 4: Antimalarial drugs prescription details.

Drugs	No. of patients	Percentages
Artesunate	21	14.89%
Chloroquine	34	24.11%
Quinine	4	2.8%
Arteether	6	4.2%
Primaquine	45	31.9%
Artemether	18	12.76%
Sulfadoxine-Pyrimethamine	13	9.21%
Total	141	

Parenteral drugs were less commonly prescribed in the treatment of malaria cases compared to oral drugs. Out of 141 prescriptions generated during the study period, chloroquine and primaquine shared major part followed by artesunate. Quinine was the least commonly prescribed drug in the treatment of malaria. (Table 4).

DISCUSSION

Our study showed males (70.69%) were more commonly affected by malaria compared to females (29.31%). *P. vivax* accounted for 38 cases (65.5%) whereas P. falciparum was found in only 8 patients (13.7%). 12 patients (20.6%) showed a mixed infection with both *P. vivax* and *P. falciparum*. But according to National Vector-borne disease control program (NVBDCP) states, *P. falciparum* constitutes the majority of disease burden in India (65%), this may be due to a variety of causes like geographical differences and climatic changes, etc. Many studies done here clearly shows a preponderance of *vivax* over *falciparum* in Karnataka.[9,10]

Majority of our patients were between 30-50 yrs (43.1%) followed by 50-65 yrs and least by 18-30 yrs. Many studies conducted on malaria patients also increased the incidence of malaria in the middle-aged people which may be due to increased exposure of malaria parasite during their work hours.[11] All the patients admitted with a history of fever which lasted for 3-20 days. other signs and symptoms on admission includes vomiting in 15 patients, the malaise in 21 patients, anemia in 18 patients, headache in 30 patients, icterus in 5 patients, gastritis in 3 patients, diarrhea in 3 patients and seizures in 2 patients.

As per the WHO definition of complicated malaria, 6 of our patients presented with complications. 4 patients with falciparum malaria and 2 patients with *vivax* malaria had complications. 2 patients had cerebral malaria, 2 patients suffered from liver dysfunction, one patient each had acute renal failure and thrombocytopenia.

Cerebral malaria is one of the most common and severe complications seen with *P. falciparum* malaria and rarely with *P. vivax* malaria. Cerebral malaria is a complex, reversible encephalopathy which may progress to coma and death if not treated well within time. Even with effective intensive care management and highly effective antimalarial drugs mortality is 10-25%.[12,13] Although exact pathogenesis is unknown a few studies suggest it might be due to microvascular obstruction by sequestrated parasitized red blood cells, microvascular thrombosis, loss of endothelial barrier function, Excessive pro-inflammatory cytokine production, and endothelial dysregulation.[14-20]

In this study, 2 of our patients with falciparum malaria developed signs and symptoms of cerebral malaria-like altered consciousness, seizures (GTCS), confusion, etc.

Another 2 patients developed hepatic dysfunction characterized by raised liver enzymes (ALT and AST), hyperbilirubinemia (Jaundice) and disorientation. Intravascular hemolysis of parasitized red blood cells is the main reason for jaundice and hepatic dysfunction. But there are some reports suggesting direct hepatic injury, sometimes referred to as “Malarial hepatitis” may also cause hepatic dysfunction.[21-23]

One patient in our study presented with acute renal failure (ARF) symptoms like rise in blood urea and creatinine. ARF can occur due to multiple reasons. The major mechanism responsible for the development of ARF is hemolysis of parasitized RBCs along with jaundice and disseminated intravascular coagulation. The activation of endothelium leads to the release of several vasoactive mediators like cytokines and interferon's which leads to a decrease in renal blood flow and finally renal ischemia and acute renal failure.[24] Volume depletion due to severe vomiting and hypotension may also have a significant role to play in the development of ARF in malaria.[25]

One of the patients with vivax malaria developed thrombocytopenia. Recently there are several reports suggesting that *vivax* malaria is no longer considered to be as mild, many severe complications especially thrombocytopenia and hepatic dysfunction can develop in *vivax* malaria.[26,27] The exact mechanism for thrombocytopenia is not known. Many studies have shown increased expression of cytokines, macrophage activation, and increased destruction of platelets by antiplatelet immunoglobulin.[28-30] Few other mechanisms proposed for

thrombocytopenia include increased oxidative stress, decreased life span of platelets and increased destruction of platelets in non-splenic sites and rarely due to increased clumping of platelets resulting in pseudo thrombocytopenia.[31-33]

Although artemisinin derivatives are more commonly preferred drugs according to new guidelines, still we found in our study chloroquine is the more preferred drug. This may be due to more cases of *P.vivax* compared to *P.falciparum* and others. Many recent studies have established chloroquine and its combination therapies are equally effective as artemisinin derivatives.[34]

Some of the limiting factors of our study include small sample size and retrospective study type. Another important factor which was evident from the study was to give equal importance in the treatment of both vivax and falciparum malaria since *vivax* is no longer considered as benign type. Many severe complications which were seen earlier in only *falciparum* malaria are now evident in *vivax* malaria. Many studies have proved that there is a significant increase in the number of severe and complicated cases with *vivax* malaria in comparison to falciparum and also increase in the morbidity as well as mortality. Further large studies with good sample size are required to study exact pathogenesis of complications seen in malaria especially with reference to *P.vivax*. We should also create awareness among the public regarding malaria, its clinical features and also educate them that if diagnosed early, treated with anti-malarial drugs on time complications can be avoided and also reduce morbidity as well as mortality.[35]

CONCLUSION

Malaria is still at rampant in India with debilitating morbidity and mortality. Studying the clinical profile of malaria with proper antimalarial drug treatment helps to curb down the complications of malaria. Every healthcare facility should follow national and international guidelines and form its in-hospital guidelines regarding proper antibiotic and antimalarial selection. This helps to reduce morbidity and mortality of malaria and helps in the sustained economic growth of the nation. Malaria is a completely curable disease.

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