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*Original Research Article.*

# Clinicopathological Study of Complicated Malaria

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## ABSTRACT

**Introduction:** Malaria is a life threatening disease caused by parasites that are transmitted to people through bites of infected female Anopheles mosquitoes. Nearly half of the world's population is at risk of malaria and most malarial cases and deaths occur in sub-Saharan Africa. In India, about 2 million confirmed malaria cases and 1000 deaths are reported annually. It remains an overwhelming problem in tropical countries, a threat to non-endemic countries and a danger to travellers. The life threatening complications resulting out of the disease leads to high fatality rate. So community awareness of the problem, early screening and diagnosis of the disease as well as effective therapy are the main stay in preventing the dreadful complications and thereby decrease mortality rates.

**Materials and Methods:** 156 malarial cases were studied out of which 96 were complicated. All patients in this study were clinically examined and investigated with routine and special diagnostic techniques; the results were recorded and tabulated.

**Results:** Out of the 96 cases of complicated malaria studied, maximum cases belonged to age group of 1-10 years with male predominance. Plasmodium falciparum infections were more common. Fever was the most common clinical presentation and found in almost all cases 94 (97.91%). CNS manifestations outnumbered other clinical complicitions and was seen in 63 (65.62%) cases followed by hypoglycemia 40 (41.66%) cases. Drug resistance was found in 22 (22.91%) cases. Death due to complicated malaria was noted in 3 (3.12%) cases.

**Conclusions:** Our study reveals that malaria is more common in children between 1-10 years of age with most common species being Plasmodium falciparum. Drug resistance is more common with Plasmodium falciparum infection and deaths were mostly due to renal complications.

**Keywords:** Cerebral, Complicated, Malaria.

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## INTRODUCTION

Malaria remains a global health problem with transmission in 91 countries. In 2016 approximately 216 million cases were registered which is 5 million more than 2015 claiming 446k lives.[1] It accounts for 85% of global infectious disease burden. Despite enormous control measures, resurgence is a problem. Added to this there are increasing problems of drug resistance of the parasite and insecticide resistance of the vectors.[2] Despite the introduction of many advanced, sophisticated, rapid and sensitive diagnostic technologies for early detection of the disease, several fatalities occur, especially with plasmodium falciparum species. Although complications are unique to *Plasmodium falciparum* infections, benign complications often occur with *Plasmodium vivax, Plasmodium malarie* and *Plasmodium ovale* infections.[3] Complicated falciparum malaria is predisposed by several factors like extremes of age, pregnancy especially in primigravida and in second half of pregnancy, immunocompromised patients on steroids and anti-cancer drugs, immunosuppressant drugs, immunocompromised patients with advanced tuberculosis and cancers, splenectomy, lack of previous exposure to malaria (no immune) or lapse immunity and preexisting organ failure.

Besides the conventional diagnostic procedures like demonstration of asexual forms of the parasite in peripheral blood smears, various rapid, sensitive diagnostic procedures like Quantitative Buffy Coat test (QBC), optimal assay, immunochromatographic tests (ICT), polymerase chain reactions, antibody detection by radioimmunoassay, flow cytometry and mass spectrometry have been employed. Still, the disease remains an overwhelming problem in the tropical developing country like India.

The vast geographical area in the coastal belt of Odisha, is highly endemic for the disease with high incidences of cerebral or falciparum malaria. Many times the disease turns fatal, because of delayed diagnosis, irregular or sub therapeutic drug treatment by the untrained health workers and also increased drug resistance of the plasmodium falciparum species to almost all antimalarial drugs. So we receive cases at an advanced stage with uni to

multiorgan failure. Hence, the present study was undertaken to evaluate the cases of complicated malaria, find out epidemiologically significant data related to various complications of the challenging disease.

## MATERIALS AND METHODS

Patients with clinical suspicion of malaria or its complications, attending the different clinical departments of S. C. B medical College Cuttack were included in the study. Data regarding age, sex, immune status of the patient, mode of presentation, endemicity and prior treatment history if any were collected. All patients were clinically examined and investigated. Patient's name, age, sex, clinical complains with duration, complications, physical and systemic examination findings were noted. Routine and special investigation findings were noted down, tabulated and calculated.

**Table 1: Age and sex distribution of different cases**

| Age group | Number of Cases | |
|---|---|---|
| (in years) | Male | Female |
| 1-10 | 14 | 12 |
| 11-20 | 6 | 3 |
| 21-30 | 5 | 8 |
| 31-40 | 12 | 4 |
| 41-50 | 8 | 2 |
| 51-60 | 3 | 2 |
| 61-70 | 10 | 1 |
| >70 | 6 | 0 |

**Table-2: Clinical findings in different cases**

| Clinical Findings | No. of Cases | Percentage |
|---|---|---|
| Anaemia | 88 | 91.66 |
| Icterus | 32 | 33.33 |
| Splenomegaly | 49 | 51.04 |
| Hepatomegaly | 32 | 33.33 |
| CNS manifestation | 63 | 65.62 |

**Table-3: Complications in different cases**

| Complications | No. of cases | Percentage |
|---|---|---|
| CNS manifestations | 63 | 65.62 |
| Severe anaemia (Hb<5gm%) | 48 | 50 |
| Hypoglycaemia | 40 | 41.66 |
| Thrombocytopenia | 30 | 31.25 |
| Hepatic dysfunction | 22 | 22.91 |
| Gastroenteritis | 16 | 16.66 |
| Renal Failure | 8 | 8.33 |

**Table-4: Malarial cases in different diagnostic methods**

| Study Methods | Positive Results | Percentage |
|---|---|---|
| Peripheral smear(PS) | 26 | 27.08 |
| ICT | 42 | 43.75 |
| QBC | 28 | 2916 |
| PS and ICT positivity | 12 | 12.05 |
| PS and QBC positivity | 8 | 8.33 |

## RESULTS

Out of the total number of 156 cases studied, 96 (61.53%) cases were diagnosed to be complicated falciparum malaria. Maximum number of cases were children between 1-10 years of age followed by older people more than or equal to 60 years of age. There was a male preponderance with male female ratio of 2:1 (Table-1). In this study, only one case of a pregnant woman having falciparum malaria complicated with severe hypoglycemia was detected that was probably due to low immunity. Fever was seen in 94(97.91%) cases, chill and rigor in 70(72.91%) cases and vomiting in 72 (75%) cases. Anaemia was seen in 88(91.66%) cases, icterus in 32(33.33%) cases, splenomegaly in 49(51.04%) cases and CNS involvement in 63(65.62%) cases (Table-2). However, severe anemia (Hb% < 5 gm%) were noted in 48 (50%) cases. CNS complications outnumbered hypoglycemia, thrombocytopenia, severe anemia, hepatic dysfunction and renal failure (Table-3).

The peripheral smear examination revealed malaria parasite in 26 (27.08%) cases. The most commonly encountered species was plasmodium falciparum 84 (70.83%) infections. Plasmodium vivax (Fig-1) infection was seen in 4(4.16%) cases and mixed infections with both plasmodium falciparum and vivax (Fig-2) was seen in 8 (8.33%) cases. The level of parasitemia was high in 3 cases (3.12%). Neutrophil containing visible malaria pigment was noted in only 2 cases. Serological tests like Immunochromatographic tests (ICT) were positive in 42 (43.75%) cases and Quantitative Buffy Coat tests (QBC) in 28 (29.16%) cases. Both smear and ICT were positive in 12 (12.05%) cases and smear and QBC were positive 8 (8.33%) cases (Table-4). Biochemical parameters of different patients revealed normal blood glucose level in 56 cases, hypoglycemia in 40 (41.66%) cases. Blood urea and serum creatinine were raised in 8 (8.33%) cases. Liver function tests were abnormal in 32 (33.33%) cases (Table-5).

Routine urine examination revealed hemoglobinuria in 2 (2.08%) of the cases studied. This is not significant, as it can occur in uncomplicated malaria. CSF findings in cases of cerebral malaria were insignificant except in 2 cases, which showed mild pleocytosis and slight increase in CSF protein level.

**Table-5: Biochemical parameters of different cases.**

| Name of the Investigation | Normal Value | No. of Cases | | |
|---|---|---|---|---|
| | | Normal Range | Decreased Value | Increased Value |
| FBS | 70-100 mg/dl | 55 | 40 | 1 |
| Blood Urea | 10-50mg/dl | 88 | - | 8 |
| Serum Creatinine | 0.5-1.2 mg/dl | 88 | - | 8 |
| Serum bilirubin | 0.2-1.0 mg/dl | 64 | - | 32 |
| Serum alkaline phosphatase | Children - 151-471 U/L<br>Adults - 60-170 U/L | 64 | - | 32 |
| AST | 5-46 U/L | 64 | - | 32 |
| ALT | 5-49 U/L | 64 | - | 32 |

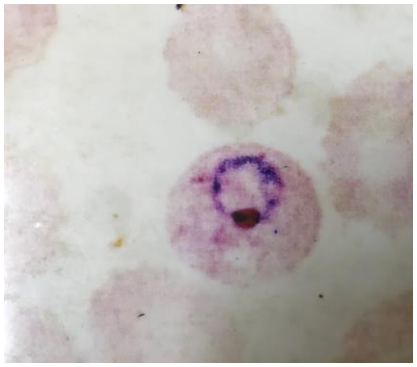

**Fig-1: Plasmodium vivax infection (x100X)**

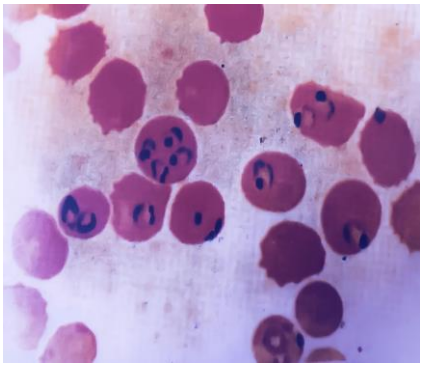

**Fig-2: Mixed infection(x40X) (Plasmodium falciparum and plasmodium vivax)**

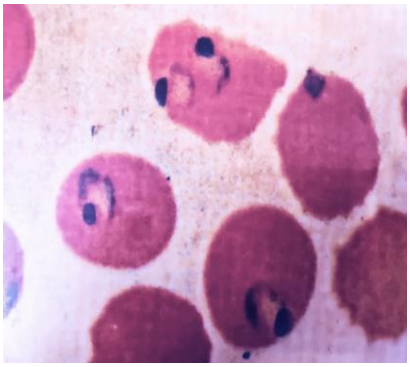

**Fig-3: Mixed infection(x100x) (Plasmodium falciparum and plasmodium vivax)**

## DISCUSSION

The global death tolls from malaria is rising and this is attributed mostly to *Plasmodium falciparum infections. Plasmodium vivax, Plasmodium malarie* and *Plasmodium ovale* infections are generally benign and complications leading to significant morbidly and mortality are uncommon. Mixed infections with both Plasmodium falciparum and Plasmodium vivax are also commonly encountered in malaria endemic areas **(Fig-3).** The case fatality of falciparum malaria is around 1% and this accounts for more than half a million deaths per year all over the world; 80% of these deaths are caused by cerebral malaria. The major complications of severe malaria include cerebral malaria, pulmonary edema, acute renal failure, severe anemia and or bleeding. Acidosis and hypoglycemia are the most common metabolic complications. Any of these complications can be fatal.[4] In many patients, multiple complications co-exist or develop in rapid succession within few hours. Cerebral symptoms were seen in 63(65.62%) cases in the present study. In contrast, Kumawat BL et al[5] noted cerebral symptoms in 11.1%, Gupta et al[6] in 8.3%, Upadhyaya and Bhalla et al[7] in 3.05% of cases. The higher incidence in the present study could be attributed to the fact that this hospital is a tertiary care referral hospital and uncomplicated cases are mostly treated in rural health centers.

Anaemia in malaria is due to lysis of both parasitized and non-parasitized RBCs compounded by bone marrow dysfunction. Anaemia is more common in falciparum malaria, as it affects RBCs of all age groups. In this study, splenomegaly was found in 49 (51.04%) cases. Kochar et al[8] noted splenomegally in 63% cases. This is mainly due to reticular hyperplasia, increased capacity to clear red cells from the circulation by Fc mediated immune mechanism and by filtration of deformed RBCs.

Hepatomegally was found in 32 (33.33%) cases. Kochar et al noted hepatomegaly in 9.10% cases.[8] The higher incidence in our case may be due to more numbers of falciparum infections.

Hypoglycemia was encountered in 40 (41.66%) cases. Upadhyaya et al reported hypoglycemia in 8.3% cases.[7] Hypoglycemia is mainly due to failure of hepatic gluconeogenesis, increased consumption by the parasite and use of quinine group of drugs.

Renal failure due to malaria was seen in 8 (8.33%) cases. It is a sensitive indicator of the prognosis in cerebral malaria. Sitprija et al noted renal failure in 6% cases.[9] Thrombocytopenia was noted in 30 (31.25%) cases. The incidence was high in adults. However, the degree of thrombocytopenia was mild in this study without any bleeding manifestations.

Gastroenteritis was seen in 16 (16.66%) cases. Gastroenteritis is common among young children with falciparum infections and is due to cytoadherence of parasitized RBCs to endothelial cells in the microvasculature of GIT.

Microscopic examination is the mainstay of malaria diagnosis. Recently, modern techniques using antigen tests or polymerized chain reactions have been developed, though not widely implemented in malaria endemic areas.[10] Immonochromatographic tests, called malaria rapid diagnostic tests (Dipsticks) are developed, results of which can be read visually. Modern rapid diagnostic test includes a combination of antigens for example, plasmodium falciparum specific antigen histidine rich protein II (HRP II) and either a plasmodium vivax specific antigen or an antigen sensitive to all plasmodium species (PLDH).

Molecular methods like QT-NASBA based on the PCR are being developed to deploy them in malaria endemic areas. Quantitative Buffy Coat (QBC) test is used to detect malaria infections. The fluorescent parasites are observed under UV light after centrifuging the blood sample in acridine orange coated capillary tubes. The test is more sensitive than conventional thick smear, but cannot differentiate the malaria species.[11]

Drug resistance was found in 22 (22.91%) cases. This high incidence is attributed primarily to the development of resistance of falciparum species to almost all antimalarial drugs with the exception of Artemisinin group of drugs.[12] Three cases succumbed to death during the study period due to renal failure.

## SUMMARY AND CONCLUSION

Malaria is a very simple disease to diagnose and treat; yet it claims more lives than other infectious diseases if not diagnosed and treated early. The above mentioned statistical data reflects the vastness of the disease, its public health importance and its enormous burden on both medical and economic infrastructure of our country as it is one of the eradicable infectious diseases. The emergence of drug resistance is a challenge. However, availability of special malaria detection kits, posting of trained laboratory personnel in malaria endemic areas can help in controlling the disease. The little effort in our institution will no doubt help the health care system team to face the life threatening complications of malaria in a better way.

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