# Clinical Profile and Outcome of Complicated *Plasmodium falciparum* Malaria

**Virendra C. patil[1], Harsha V. Patil[2]**

[1]*Department of Medicine, Krishna Institute of Medical Sciences University (KIMSU) Dhebewadi Road, Karad, Satara District, Maharashtra – 415 110, India*

*2Department of Microbiology Krishna Institute of Medical Sciences University (KIMSU), Dhebewadi Road, Karad, Satara District, Maharashtra – 415 110, India.*

## ABSTRACT

**Context:** Complicated *Plasmodium falciparum* Malaria is a syndrome and a disease of protean, clinical manifestations including jaundice, ARF, ARDS and multi-organ failure. **Aims:** The objectives of the present study are to study clinical features, complications and factors affecting outcome of patients with complicated *P. falciparum* Malaria. **Settings and Design:** This retrospective descriptive study was conducted at tertiary care centre in western Maharashtra from January 2010 to December 2010. **Methods and Material:** Total 73 patients with complicated *P. falciparum* malaria who presented with fever having positive trophozoites of *P. falciparum* in blood smear were included. SPSS (version-10) software was used for all statistical calculations. **Results:** A total 73 patients had complicated *P. falciparum* malaria with 52 were males and 21 were female patients. Total 9 (12.32 %) patients were presented with shock as a presenting feature. Four (5.47 %) patients had hypoglycaemia at the time of admission. Total 43 (58.90 %) patients had jaundice, 37 (50.68 %) had anaemia, 28 (38.35 %) had cerebral malaria, 7 (9.58 %) had acute renal failure, 5 (6.84 %) had ARDS and 5 (6.84 %) had thrombocytopenia. Total 46 patients had single complication in the form of cerebral malaria 14 (19.17 %), jaundice 15 (20.54 %) and anaemia 16 (21.91 %). Total 14 patients had two complications in the form of jaundice with ARF 02 (2.73 %) with one (50 %) death and jaundice with anaemia 12 (16.43 %). Total 9 (12.32 %) patients had three complications in the form of cerebral malaria with jaundice with anaemia with 3 deaths (33.33 %). Total 5 (6.84 %) patients had multiple complications in the form of cerebral malaria with ARF with ARDS with thrombocytopenia with 4 (80 %) death. Case fatality rate was 10.95 %. The case fatality rate with ARDS was 80 % (4/5), with ARF was 57.14 % (4/7) and with cerebral malaria it was 25 % (7/28). Case fatality rate was highest in patients with pulmonary complication (ARDS) compared to ARF, cerebral malaria, jaundice and anaemia with 'p' $< 0.001$. **Conclusions:** Acute renal failure and ARDS were least common presentation with poor outcome. In present study most common presentation was with jaundice and anaemia next to that was cerebral malaria. The case fatality rate of *P. falciparum malaria* was 10.95 %. Overall case fatality rate was highest with multi-organ dysfunction (80 %). Unusual early renal and pulmonary complications were the presenting features of complicated *P. falciparum malaria* were observed in present study. Presenting feature as a shock was invariably associated with either ARDS or ARF with high mortality. This study highlights the burden of complicated malaria including multi-organ dysfunction in western Maharashtra.

**Key words:** *Plasmodium falciparum*, ARF, ARDS, multi-organ failure

## INTRODUCTION

Malaria is one of the most common parasitic diseases causing morbidity and mortality in India. Malaria cases have been fluctuating between 2 to 3 million with about 1000 deaths annually. *P. falciparum* cases fluctuate between 1 to 1.2 million; thus *falciparum* malaria accounts for 50 % malaria in the country. India contributes about 70 % of malaria in the South East Asian Region of WHO. Although annually India reports about two million cases and 1000 deaths attributable to malaria, there is an increasing trend in the proportion of *Plasmodium falciparum* as the agent. The mortality in Malaria is due to *Plasmodium falciparum*. The considerable mortality and morbidity in *falciparum* malaria is due to its protean manifestation, multi-organ involvement and delay in diagnosis and

**Address for correspondence:** Dr. Virendra C. Patil

Krishna Institute of Medical Sciences University
Dhebewadi Road, Karad, Satara District
Maharashtra-415 110, India

E-mail: virendracpkimsu@rediffmail.com

**DOI:** 10.5530/ijmedph.2.1.12

failure of administration of treatment promptly. The pattern of clinical presentation of severe malaria has also changed and while multi-organ failure is more frequently observed in *falciparum* malaria. Recently there is a changing trend not only in the clinical manifestations but also the complications, and more and more patients are presenting with ominous systemic manifestations.[1,2] All cases of *falciparum* malaria are potentially severe and life threatening medical emergency. A major reason for progression from mild through complicated to severe disease is missed or delayed diagnosis. Severe disease is treated with parenteral administration of adequate, safe doses of appropriate anti-malarial drugs. Supportive management of complications such as coma, convulsions, metabolic acidosis, hypoglycemia, electrolyte disturbances, renal failure, secondary infections, bleeding disorders and anemia are also important. Severe and complicated malaria is characterised by multi-organ involvement including acute lung injury (ALI), acute respiratory distress syndrome (ARDS) and ARF. Recent years have witnessed a multi-organ failure, ALI and ARDS are being increasingly reported in *falciparum* malaria.[3] So far there is scanty literature and published studies on complicated *P. falciparum* malaria in western Maharashtra.

## SUBJECTS AND METHODS

This study was a single centre retrospective observational study on complicated *P. falciparum* malaria conducted at Krishna institute of medical sciences karad, Maharashtra India. The objectives of the present study are to study clinical features, complications and factors affecting outcome of patients with complicated *P. falciparum* Malaria. This study is approved by ethical committee Krishna institute of medical sciences University Karad. Consecutive adult patients with age > 18 years with smear positive *P. falciparum malaria* with various complications admitted to medical wards and intensive care unit, from January 2010 to December 2010 were included in this retrospective study. Total 1673 patients were admitted with history of fever due to various etiologies. Total 203 (12.13 %) patients were admitted with *P. vivax* malaria and mixed infections. Total 73 (35.96 %) patients were included in present study with complicated *P. falciparum* malaria. As the coexistence of other diseases may influence the outcome of complicated malaria, patients with diseases like diabetes mellitus, chronic renal failure, chronic liver disease, rheumatic heart disease, coronary artery disease, and associated infections like pneumonia, urinary tract infection, leptospirosis, H1N1 and viral hepatitis were excluded. Cerebrospinal fluid analysis, abdominal ultrasound, chest radiograph, and serological markers for viral hepatitis were done to exclude these diseases. All patients who had a positive blood smear for *P. Falciparum* Malaria were included in this study. Patients who are peripheral smear negative but treated with anti malarial drugs (so called clinical Malaria) and other malarias (*Plasmodium vivax, Plasmodium ovale, Plasmodium malariae*) were excluded.

On admission, peripheral blood smears were collected for Giemsa staining and subsequently every 12 hours to assess parasitemia. Parasite count with stage identification and index was determined (Figure 1). Blood was collected for estimation of glucose, urea, creatinine, sodium, albumin, bilirubin, aspartate amino transferase (SGPT), alanine amino transferase (SGOT), and for haematological investigations such as haemoglobin, platelet count, total leukocyte count, and prothrombin time (PT). Arterial blood gas analysis in patients with respiratory distress was done in 16 patients. The pH, $PCo_2$, and $PO_2$ were gauged and chest radiograph was done in 5 cases for diagnosis of respiratory distress and pulmonary edema (Figure 2). The diagnosis of malaria was made with detection of asexual form of *P. falciparum* from Giemsa stained peripheral blood smear.[2] Patient with *P. falciparum* asexual parasitaemia and no other obvious cause of symptoms, the presence of one or more of the following clinical or laboratory features classifies the patient as suffering from severe malaria.

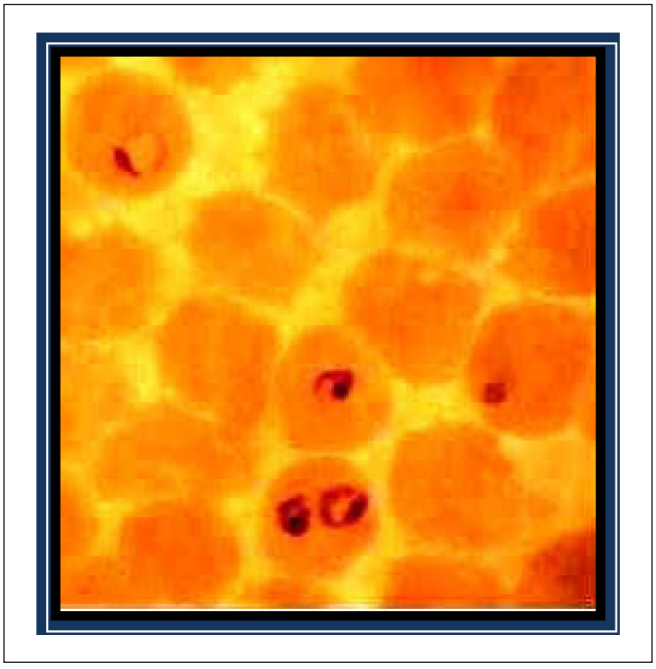

**Figure1:** Ring stage trophozoites of *P. falciparum*

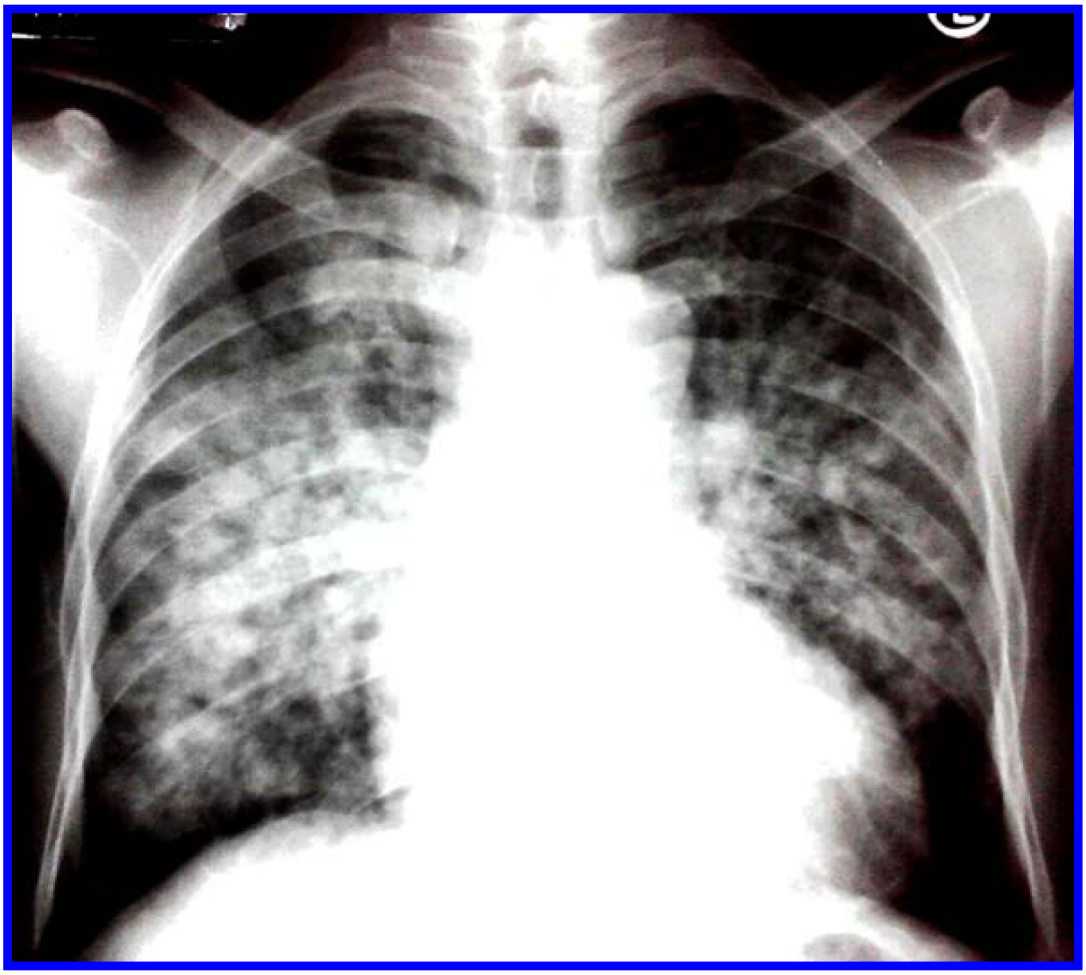

**Figure 2:** Chest radiograph showing bilateral alveolar pulmonary infiltration with ARDS in a patient with complicated *P. falciparum*

Severe malaria was diagnosed according to the guidelines of World Health Organization. Cerebral malaria was diagnosed when a patient had unarousable coma using Glasgow Coma Scale with exclusion of other encephalopathies with multiple convulsions – more than two episodes in 24 hours. Renal failure, jaundice, hypoglycemia, and severe anemia were diagnosed when s. creatinine was more than 2.0 mg/dl., s. bilirubin was more than 2.0 mg/dl., random blood glucose was less than 60 mg/dl., and haemoglobin was less than 7.0 gm/dl respectively. The metabolic acidosis was labeled if plasma bicarbonate < 15 mmol/l. Circulatory collapse (hypotension) had been defined as systolic blood pressure (BP) < 90 or a fall in BP of more than 40 mm of Hg unresponsive to fluid administration. Respiratory distress was defined when patient had tachypnoea with or without pulmonary edema (radiological).[3]

Parasite index (PI): Number of parasites per 1000 RBC's e.g. one field 100 RBC's then 10 fields 1000 RBC's are studied (Parasitised /1000 RBC's (10–100 %). For 1000 RBC's number of parasites says for example 40 then the percentage are 4. Intensity of infection was measured in thin films i.e., percentage of RBC.

Patients with one complication were grouped under single complication, two complications, three complications and multiple complications. Onset time, resolution time, duration, and progression of complications as well as duration of hospital stay were determined. Assuming fever as the onset of clinical malaria, the interval of fever to the onset of various complications has been defined as the onset time of the respective complications. Thus onset time of coma, renal failure, anemia, hypoglycemia, jaundice, respiratory distress, and hypotension were

determined. The outcome was binary i.e. either recovery or death. Severe malaria is a medical emergency. Airway secured in unconscious patient IV infusion of dextrose normal saline started with CVP monitoring. In unconscious patients lumbar puncture and CSF study to exclude meningitis (bacterial/viral). Patients were examined and assessed twice daily until full recovery or death. All patients were treated with intravenous quinine dihydrochloride at a loading dose of 20mg/kg administered over 3 hrs. Subsequent dose of 10 mg/kg administered over 2 hrs every 8 hrs in a 10 % dextrose solution until the patient could take medication orally. Treatment was continued for 7 to 10 days. Complications such as anemia, hypoglycemia, convulsion, renal failure, jaundice, respiratory failure and circulatory collapse were treated according to the standard protocol. The data were pooled, computerized, and analyzed by SPSS (Version-10) software. Patient characteristics and the outcome of interest and relative risk and their corresponding 95 % confidence interval were calculated. Prevalence rates were given in percentage. Various numbers are given as mean and standard deviation ± 1 SD. For continuous variable, mean values were compared using two sample't' tests for independent samples. Categorical variables have been compared by using $\chi^2$ (Chi-square) test. The probability $< 0.05$ was considered as significant. Correlations of complication with laboratory variable were determined using $r^2$ and multiple linear regression analysis. Correlation (r): r = 0.8 (high correlation coefficient), r = 0.4–0.7 (moderate correlation), and r = 0.3 and above (low correlation coefficient).

## RESULTS

Out of total 1673 patients with history of fever, 203 patients were with uncomplicated P. *falciparum*, *P. vivax* malaria and mixed infections. Total 73 patients were included in present study with complicated *P. falciparum* malaria. The present study was conducted on 73 adult patients with complicated *P. falciparum* malaria of both sexes admitted during the year 2010 (January to December 2010). Data is collected from Medical record sections of Krishna institute of medical sciences Karad. During the retrospective study period, 73 patients who proved parasitiologically positive for *P. Falciparum* were studied and following observation were made. Total 52 (71.23 %) were males and 21(28.76 %) were female patients with mean age of 33±14 years and 27±16 years for females. Total 57 (78.08 %) cases were in August – December. Out of total 73 patients 39 (53.42 %) patients were critically ill and treated in intensive care unit. Total 34 (46.57 %) were managed in medical wards. Total 8 (10.95 %) patients had remittent 13 (17.8 %) had continuous and 52 (71.23 %) had intermittent type of fever. Headache was present in 38 (52.05 %) patients. Generalized weakness, nausea and anorexia were present in 61(83.56 %) patients. Vomiting was present in 32 (43.83 %) patients. Total 15 (20.54 %) patients were in delirium and 9 (12.32 %) patients were unconscious. Total 4 (5.47 %) patients had generalized tonic clinic convulsions and 5 (6.84 %) had meningeal signs. Total 2 (2.73 %) patients had papilloedema. Four (5.47 %) patients had hypoglycemia at the time of admission. Total 43 (58.90 %) patients had jaundice. Total 9 (12.32 %) patients had hypotension. Oliguria was present in 7 (9.58 %) patients as a presenting feature. Breathlessness and cough was present in 5 (6.84 %) patients with low SpO2. Total 3(4.1 %) patients had bleeding tendency in the form of epistaxis, malena and hematemesis. Spleenomegaly was present in 31(42.46 %) patients and hepatomegaly was present in 22 (30.13 %) patients. Total 37(50.68 %) patients had pallor (Table 1 & Figure 3). The mean and standard deviation (±1) of laboratory parameters is shown in table number 2. Total 5 patients had parasitic index <1 % , 17 had 1–2 % , 13 had 2–6 % and 16 had 6-8 %. Total 4 patients had parasitic index 8–10 % , 6 had 10–20 % , 5 had 20–40 % and 7 had >40 %. There was no statistical significance of parasitic index and mortality among index of 1–8 % and 8–40 %. (Table 3)

Total 43 (58.90 %) patients had jaundice, 37 (50.68 %) had anemia, 28 (38.35 %) had cerebral malaria. Total 9 (12.32 %) patients were presented with shock as a presenting feature. Total 7 (9.58 %) had acute renal failure, 5 (6.84 %) had acute lung injury (ALI)/ acute respiratory distress syndrome (ARDS) and 5 (6.84 %) had thrombocytopenia. In present study most common presentation was with jaundice and anemia next to that was cerebral malaria. Acute renal failure and ARDS were least common presentation with poor outcome and high mortality. Total 46 patients had single complication in the form of cerebral malaria 14 (19.17 %), Jaundice 15 (20.54 %) and anemia 16 (21.91 %) with no mortality. Total 14 patients had two complications in the form of jaundice with ARF 02 (2.73 %) with one (50 %) death and jaundice with anaemia 12 (16.43 %). Total 9 (12.32 %) patients had three complications in the form of cerebral malaria with jaundice with anemia with 3 deaths (33.33 %). Total 5 (6.84 %) patients had multiple complications in the form of cerebral malaria with ARF with ARDS with thrombocytopenia with 4 (80 %) death. Total 28 (38.35 %) had isolated cerebral malaria without other organ involvement of which 4 (54.79 %)

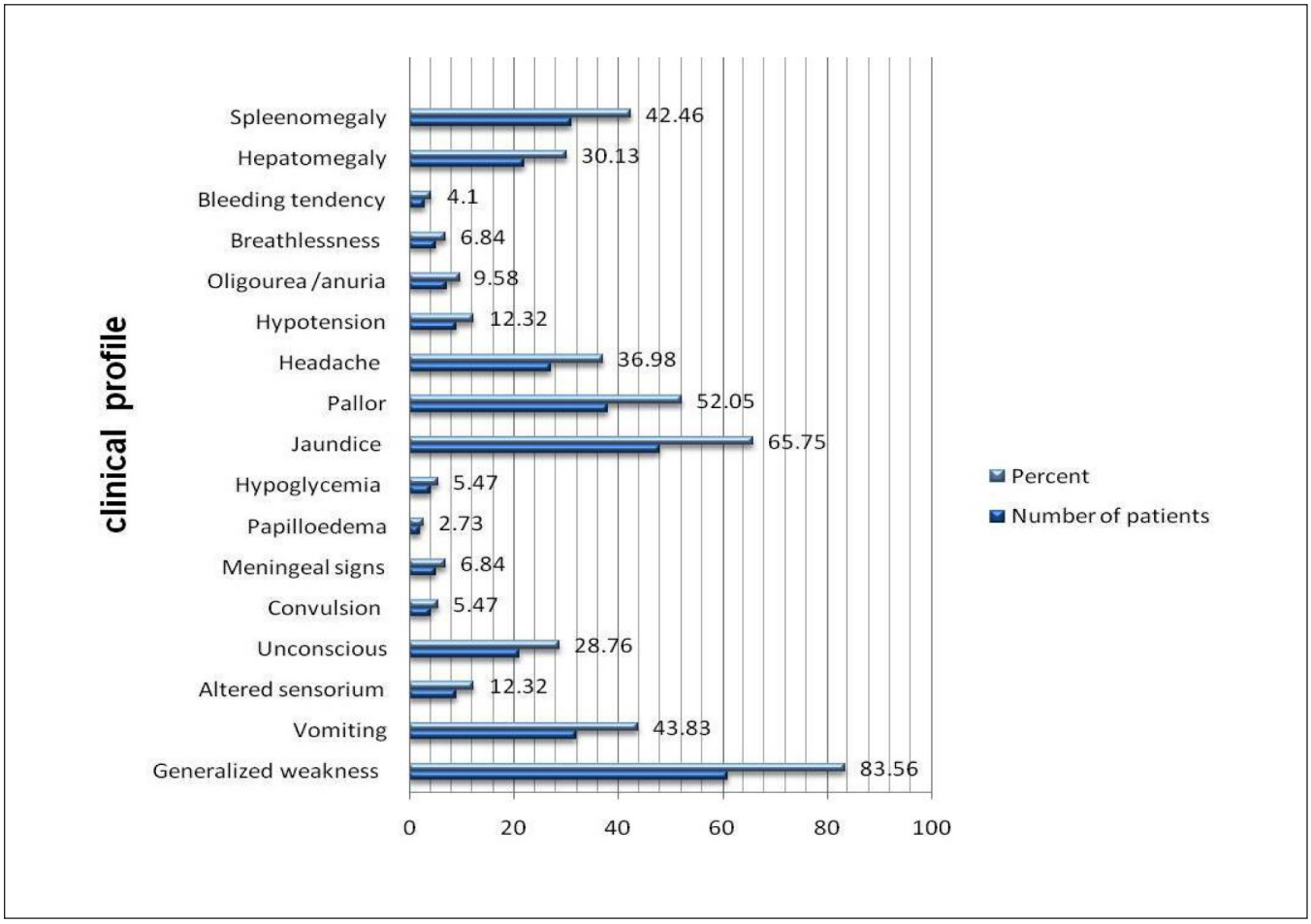


**Figure 3:** Clinical profile of complicated *P. falciparum* malaria

**Table 1: Clinical profile of *P. falciparum* complicated malaria**

| Symptom | Number of patients | Percent |
|---|---|---|
| Fever | | |
| 1. Intermittent | 52 | 71.23 |
| 2. Remittent | 13 | 17.80 |
| 3. Continuous | 08 | 10.95 |
| Generalized weakness nausea/anorexia | 61 | 83.56 |
| Generalized weakness nausea/anorexia | 61 | 83.s6 |
| Vomiting | 32 | 43.83 |
| Altered sensorium | 9 | 12.32 |
| Unconscious | 21 | 28.76 |
| Convulsion | 4 | 5.47 |
| Meningeal signs | 5 | 6.84 |
| Papilloedema | 2 | 2.73 |
| Hypoglycemia | 4 | 5.47 |
| Jaundice | 48 | 65.75 |
| Pallor | 38 | 52.05 |
| Headache | 27 | 36.98 |
| Hypotension | 9 | 12.32 |
| Oligurea | 7 | 9.58 |
| Breathlessness | 5 | 6.84 |
| Bleeding tendency | 3 | 4.10 |
| Hepatomegaly | 22 | 30.13 |
| Spleenomegaly | 31 | 42.46 |

required mechanical ventilation. Total 7 had oliguric renal failure and all of them required hemodialysis of which 2 (28.57 %) were recovered 5(71.42 %) died. Total 5 patients had pulmonary involvement in the form of ARDS of which all required artificial ventilator of which 4 (80 %) succumbed (Table 4 & figure 4). Total 21 patients required blood transfusions. Out of 21 with severe anemia patients 15 (71.42 %) received packed cell transfusions and 6 (28.57 %) required whole blood transfusion for correction of anemia. Total 8 (10.95 %) patients required platelet transfusions in the form of single donor platelets (SDP) and vitamin K for treatment of thrombocytopenia and DIC. At the time of admission total 9 (12.32 %) patients had shock which was treated by fluid resuscitation and inotropic agent support under CVP monitoring. Out of total 9 patients with hypotension 7 (77.77 %) have developed acute renal failure. Total 9 patients required artificial ventilator for ARDS and or aspiration pneumonitis, associated with seizures, for period of 7 days ± 2. Total 7 patients developed acute renal failure required renal

**Table 2: Mean and standard deviation of laboratory parameters of complicated *P. falciparum* malaria.**

| Laboratory parameter | Mean | Standard deviation |
|---|---|---|
| Hb (gm%) n=37 | 4.1 | ±0.7 |
| TC (cmm) n=73 | 9900 | ±2500 |
| Platelet count (cmm) (n=5) | 75,000 | ±28,000 |
| BUL (mg%) n=7 | 89 | ±37 |
| Sr. Creatinine (mg%) 7 | 6.7 | ±3.9 |
| Total bilirubin (mg/dL.) (43) | 10.9 | ±5.3 |
| SGOT (U/L) n=43 | 185 | ±39 |
| SGPT (U/L) n=43 | 173 | ±29 |
| Alpo4 (n=43) | 198 | ±23 |
| Prothrombin time (n=43) | 1.9 | ±0.4 |
| pH (n=16) | 6.4 | ±0.34 |

**Table 3: Parasite Index in patients with *P. falciparum* malaria**

| **Parasite Index** | **<1%** | **1 –2%** | **2 –6%** | **6 –8%** | **Total (n=73)** |
|---|---|---|---|---|---|
| No. of patients | 5 | 17 | 1 β | 16 | [death n=6 (11.76%)] |
| **Parasite Index** | **8 –10%** | **10–20%** | **20–40%** | **> 40%** | |
| No. of patients | 4 | 6 | 5 | 7 | 22 [death n=2 (9.09%)] |

'p' insignificant.

**Table.4: Clinical presentation and complications of complicated malaria**

| Number of complications | Duration of hospital stay (days) | Total patients (n= 73) | Death (n= 8) |
|---|---|---|---|
| Single complication | | | |
| Cerebral malaria | 9 (±3) | 14 (19.17%) | Nil |
| Jaundice | 8 (±4) | 15 (20.54%) | Nil |
| Anemia | 6 (±3) | 16 (21.91%) | Nil |
| Two complications: | | | |
| Jaundice with ARF | 5(±2) | 02 (2.73%) | 01 (50%) |
| Jaundice with anemia | 11(±3) | 12 (16.43%) | Nil |
| Three complications: | | | |
| Cerebral malaria with jaundice with anemia | 13 (±3) | 09 (12.32%) | 03 (33.33%) |
| Multiple complications | | | |
| Cerebral malaria with ARF with ARDS with thrombocytopenia | 7(±4) | 05 (6.84%) | 04 (80%) |
| Total | 15(±7) | 73 | 08 (10.95%) |

'p' < 0.001.

replacement therapy in the form of hemodialysis (9±4 cycles). Two patients those who survive after dialysis required 45 ± 5 days to normalise renal parameters. Total 16 patients had acidic pH of which 9 (56.25 %) had metabolic acidosis and 7 (43.75 %) had respiratory acidosis which was corrected haemodialysis, artificial ventilator and/or sodium bicarbonate supplementation. In single complication the mean duration of hospital stay in patients with cerebral malaria was 9 (±3) days, for jaundice 8 (±4) days and with anemia it was 6 (±3) days. Patients with two complications the mean duration of hospital stay was 5(±2) days for jaundice with ARF and 11(±3) days for Jaundice with anemia. In patients with three complications the mean duration of hospital stay was 13 (±3) days for cerebral malaria with jaundice with anemia. Patients with multiple complications the mean duration of hospital stay was 7(±4) days [cerebral malaria with ARF with ARDS with thrombocytopenia]. Overall mean duration of hospital stay was 15 days ±7 days. Out of 73 patients admitted and treated for complicated *P. falciparum* malaria 65 (89.04 %) patients were discharged in ambulatory state after recovery from complications and parasitic clearance. (Table 4)

Out of total 28 patients with cerebral malaria 7 (25 %) succumbed. Total 5 patients developed ARDS of which 4 (80 %) succumbed. Total 7 patients developed ARF of which 5 (71.42 %) succumbed. Case fatality rate was significantly high with ARDS and ARF compared to cerebral malaria with 'p'< 0.001 (odds ratio: 3.12). (Table 5 & figure 5)

Total 8 patients succumbed with complicated *P. falciparum* malaria with case fatality rate of 10.95 %. In univariate analysis overall case fatality rate was highest with multi-organ dysfunction compared to single, two and three complications which was statistically significant ('p'< 0.02). The case fatality rate with ARDS was 80 % (4/5), with ARF was 57.14 % (4/7) and with cerebral malaria it was 25 % (7/28). Case fatality rate was highest in patients with ARDS compared to ARF, cerebral malaria, jaundice and anemia with 'p' < 0.001 (Table 4). Patients presented with hypotension had more incidence of ARF and ARDS (8/9) compared to with normotension ('p' = 0.25) with an odds ratio of 2.31. Mortality rate was high with patients presented after 5 days (7/8) of starting symptoms compared to those who presented before 5 days ('p' < 0.05) with an odds ratio of 1.87. Duration of hospitalisation was positively correlated with sr. creatinine (+0.08), sr. bilirubin (+0.03), haemoglobin (+0.021) and negatively correlated with $SpO_2$ (−0.93), blood sugar level (−0.5), blood pressure (−0.87).

In *multivariate analysis* (MANCOVA) late presentation, ARF, hypotension, ARDS, thrombocytopenia, absences of spleenomegaly, convulsions and hypoglycemia were associated with prolonged hospital stay, high mortality and poor outcome ('p' = 0.001). Age, gender, parasitic index and total serum bilirubin were not statistically significantly associated outcome of complicated *P. falciparum* malaria.

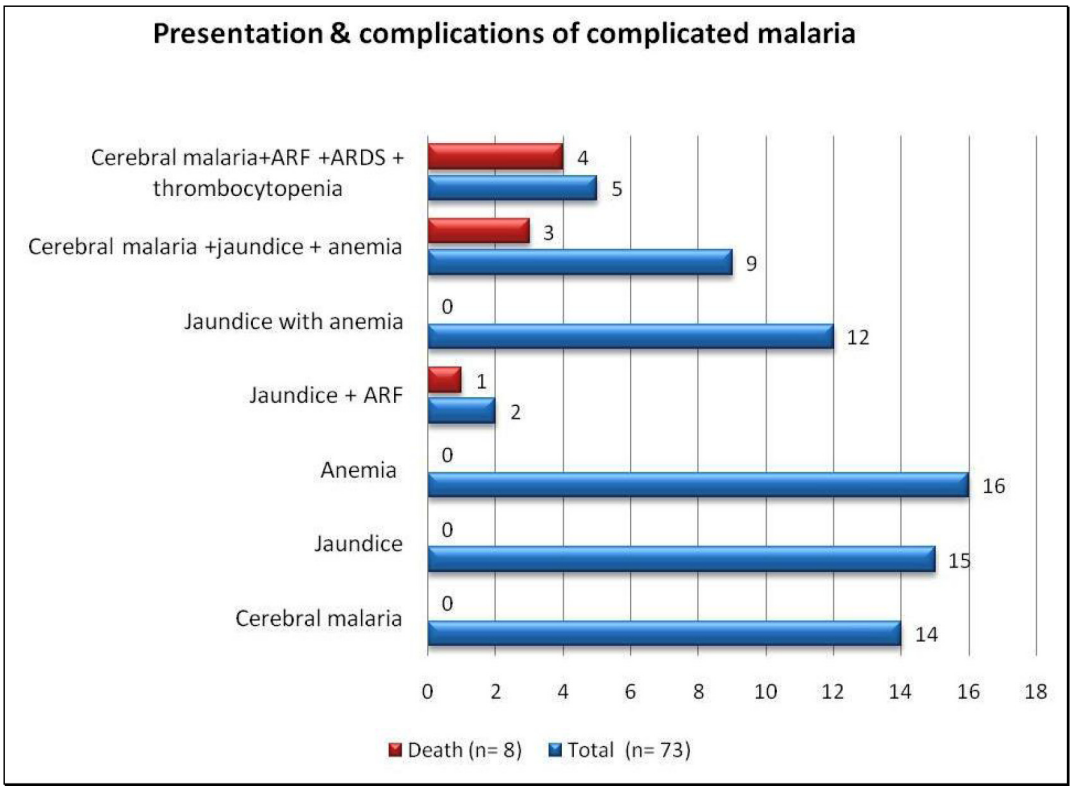


**Figure 4:** Clinical syndrome and complications of complicated *P. falciparum* malaria

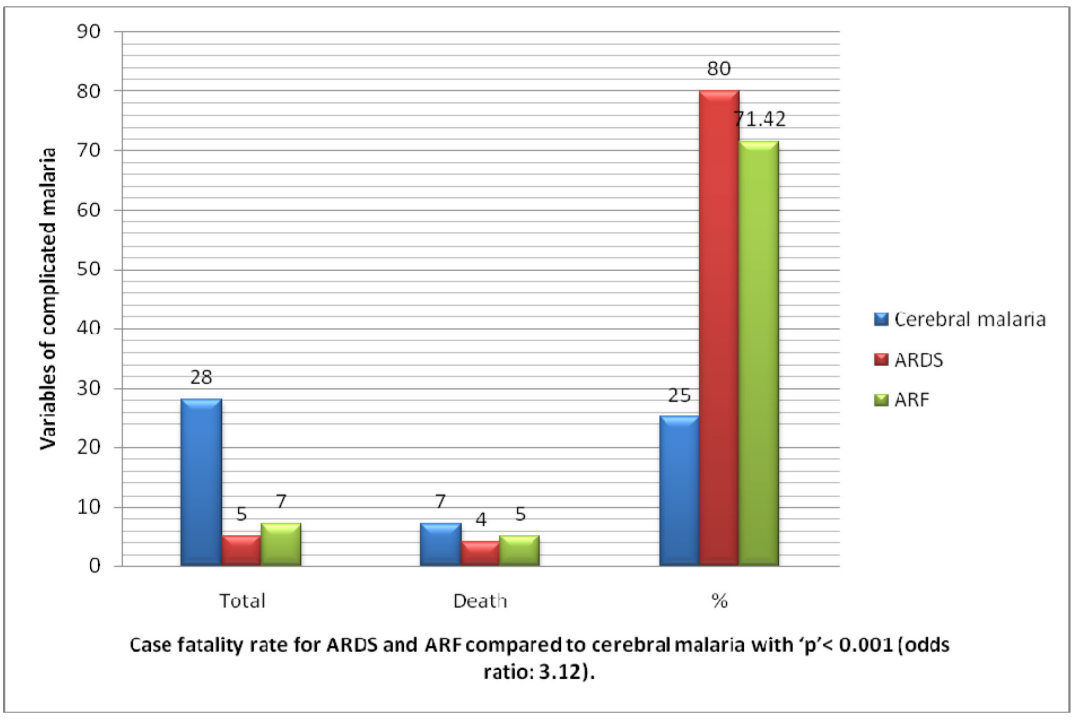


**Figure 5:** Case fatality rate amongst the complications of complicated malaria

**Table 5: comparison of case fatality rate amongst the complications of complicated malaria**

| Variable | Total | Death |
|---|---|---|
| Cerebral malaria | 28 | 7 (25%) |
| ARDS | 5 | 4 (80%) |
| ARF | 7 | 5 (71.42%) |

Case fatality rate for ARDS and ARF compared to cerebral malaria with 'p'< 0.001 (odds ratio: 3.12).

## DISCUSSION

In present study most common presentation was with jaundice and anemia next to that was cerebral malaria. Acute renal failure and ARDS were least common presentation with poor outcome and high mortality. ARDS with ARF with shock was main highlight of present study with high case fatality rate (80 %). Total 46 patients had single complication in the form of cerebral malaria 14 (19.17 %), Jaundice 15 (20.54 %) and anemia 16 (21.91 %) with no mortality. Total 14 patients had two complications in the form of jaundice with ARF 2 (2.73 %) with one (50 %) death and jaundice with anemia 12 (16.43 %). Total 9 (12.32 %) patients had three complications in the form of cerebral malaria with jaundice with anemia with 3 deaths (33.33 %). Total 5 (6.84 %) patients had multiple complications in the form of cerebral malaria with ARF with ARDS with thrombocytopenia with 4 (80 %) death. Total 8 patients were died with complicated *P. falciparum* malaria with case fatality rate of 10.95 %. The parasitic index was not correlating with mortality associated with *P. falciparum* malaria. ARF, ARDS and thrombocytopenia are the uncommon presenting features in present study. Overall case fatality rate was highest with multi-organ dysfunction compared to single, two and three complications which was statistically significant ('p'< 0.02). Case fatality rate was highest in patients with ARDS compared to ARF, cerebral malaria, jaundice and anemia with 'p' < 0.001. Out of 9 patients presented with shock, 8 succumbed and were associated ARF with ARDS.

We compared our results with various studies with different geographic area. *Kochar et al.* in their study of 532 patients with *P. falciparum* malaria observed that, cerebral malaria (25.75 %), hepatic involvement (11.47 %), spontaneous bleeding (9.58 %), severe anemia (5.83 %), ARDS (3 %) and renal failure (2.07 %) were the important manifestations.[4] Overall mortality was 11.09 %. Morality was highest in ARDS (81.25 %) followed by severe anemia (70.97 %), renal failure (45.45 %), jaundice (36.06 %) and cerebral malaria (33.57 %). Mortality was very high (82.35 %) in those persons who presented with more than 3 syndromes together. These findings are comparable with our study were case fatality rate with multi-organ dysfunction was 80 % with ARDS and ARF. *Mishra SK et al.* in their study stated that the severe malaria is invariably caused by *Plasmodium falciparum* and acute renal failure and jaundice are more common among adults.[5] The case-fatality rate due to severe malaria is 10-15 % in spite of therapy but it increases in the presence of renal failure or respiratory distress (pulmonary edema or ARDS). In present study overall case fatality rate was (10.95 %) and patients with multi-organ dysfunction it was 80 %. *Mishra et al.* in their study in eastern India found that, the most common presenting symptoms were fever (97.7 %), vomiting (54.6 %), headache (30.8 %) and seizures (17.1 %).[6] Total 62.4 % of the cases had associated severe complications: jaundice (47.5 %), acute renal failure (28.9 %), and/or severe anemia (9.7 %). Overall, 175 (23 %) of the cases were fatal, mortality being particularly high (59 %) among those with multi-organ failure. These findings are comparable with present study in which total 5 (6.84 %) patients had multiple complications in the form of cerebral malaria with ARF with ARDS with thrombocytopenia with 4 (80 %) death. Total 8 patients were died with complicated *P. falciparum* malaria with case fatality rate of 10.95 %. Overall case fatality rate was highest with multi-organ dysfunction compared to single, two and three complications with which was statistically significant ('p'< 0.02). The case fatality rate with ARDS was 80 % (4/5), with ARF was 57.14 % (4/7) and with cerebral malaria it was 25 % (7/28). Case fatality rate was highest in patients with ARDS compared to ARF, cerebral malaria, jaundice and anemia with 'p' < 0.001. *Kochar et al.* in their prospective study in Bikaner, Rajasthan (northwest India) 2001 found that jaundice (58.85 %) followed by severe anemia (26.04 %), bleeding tendencies (25.52 %), shock (10.94 %), cerebral malaria (10.94 %), renal failure (6.25 %), ARDS (2.08 %) and hypoglycemia (1.56 %). [7] Similarly, the important cause of mortality in 2001 was multiple organ dysfunction syndrome (71.10 %) with predominant presentation of jaundice and renal failure. These findings are comparable with present study were 05 (6.84 %) patients presented with ARDS with ARF with cerebral malaria with case fatality rate of 80 %. *Jain et al.* in their study of 199 patients with cerebral malaria (CM) in central India, found that presentation with jaundice (26 %), acute renal failure (22 %), respiratory distress (22 %), severe malaria anemia (18 %), hypotension (17 %), hepatic encephalopathy (7.0 %), and hematuria (5 %).[8] Mortality was high among adults with multiple organ failures. Overall case fatality rate was 21 %. These findings are similar to our study were 05 (6.84 %) with ARDS and 7 (9.58 %) with ARF and all ARDS were

concurrently associated with ARF and hypotension. *Chishti et al.* in their study of 64 patients of *Plasmodium falciprum* infections found that 90.63 % developed one or more complications.[9] The most common complication was anemia accounting for 76.56 % followed by cerebral malaria (59.38 %). Other lesser complications were leucopenia (15.63 %), thrombocytopenia (26.56 %), and adult respiratory distress syndrome (6.25 %). Total 12.5 % died due to development of multiple complications like severe haemolytic anemia, haemolytic jaundice, cerebral malaria and acute renal failure. These findings are comparable with our study in which prevalence of cerebral malaria, ARF and ARDS with mortality of 10.95 % were comparable. *Mohanty et al.* in their study 608 *Plasmodium falciparum* malaria patients with severe malaria had mortality of 13.65 %. [10] Acute renal failure, jaundice and respiratory distress were the common complications in their study, which is comparable with our results. *Mishra et al.* in their study found that 11.8 % patients had acute renal failure and hypotension was encountered in about a third.[11] The mortality in presence of acute renal failure was high ($p < 0.001$). In our study all the patients who developed ARF had hypotension. *Harris VK et al.* in their study observed that 28 % had cerebral malaria and 37 % had hyperbilirubinemia with mortality of 10 % was seen only in *P. falciparum* malaria.[12] High incidence of hepatic involvement and hepato-renal failure were the unusual features. *Prakash J et al.* in their study found that out of 577 cases of ARF 74 (79.61 %) were with *P. falciparum* with mortality of 15.7 %. [13] *Kanodia KV et al.* in their 100 patients with malaria induced acute renal failure found that, *P. falciparum* was reported in 85 % with oligo/anuria was present in 82 % and 78 % of the patients required haemodialysis.[14] Sixty four percent of the patients recovered completely, 10 % incompletely, and 5 % developed chronic kidney failure; mortality occurred in 21 % of the patients. Similarly in our study all 7 patients required hemodialysis of which 2 were recovered near total and 5 succumbed. *Mehta KS et al.* reported 16 patients with *P. falciparum* had ARF necessitating dialysis.[15] They stated that the severe ARF, DIC and ARDS were poor prognostic factors in complicated *P. falciparum* malaria. These findings are similar to our results. *Maheshwari A et al.* stated that, the prognosis of malarial acute renal failure is favorable with mortality rate of 18.5 % and with multi-organ failure was 33.3 %.[16] These findings are comparable with our study. *Krishnan et al.* in their study found that, the patients with one or no organ failure died (6.8 %), whereas mortality rate increased to 48.8 % in 129 patients with multiple organ failure.[17] Overall mortality rate was 24.6 %. Malaria is an important cause of multi-organ failure in India. Mortality rate is 6.4 % when one or fewer organs fail but increases to 48.8 % with failure of two or more organs. These findings are similar to present study. Considering increasing trend of multi-organ dysfunction in complicated malaria and various other diseases, there is pressing need of development of emergency medicine faculty in urban as well as rural India to reduce morbidity and mortality. This study highlights the ARDS or ALI and ARF is main factors predicting mortality amongst multi-organ failure in complicated *falciparum* malaria.

## CONCLUSIONS

Present study highlights the burden of complicated *P. falciparum* malaria in western Maharashtra with mortality rate of 10.95 %. Mortality rate was significantly high with multi-organ involvement (80 %). Unusual early renal and pulmonary manifestations were presenting features of complicated *P. falciparum* malaria with high mortality in present study. There was co-existence of ARF with ARDS with hepatic dysfunction. All the patients with ARF and ARDS had shock as a presenting feature. ARF necessitating daily dialysis was required in 100 % of patients presented with ARF. Early diagnosis and prompt treatment will reduce the mortality due to malaria. Early recognition of pulmonary involvement and timely intubation and artificial ventilation is vital to improve outcome of complicated *P. falciparum* malaria. Multi-organ failure was the commonest cause of death. Currently, high quality intensive care, early institution of artificial ventilation and daily intensive renal replacement therapy and avoidance of nephrotoxic drugs are standard practice of the prevention and management of ARDS with ARF. Mainstay of treatment consists of appropriate anti-malarial drug therapy, fluid replacement and renal replacement therapy. Severe ARF, thrombocytopenia, hypotension and ARDS were poor prognostic factors in patients with *P. falciparum* infection in present study. The patients with ARDS should be managed in an intensive care unit. Careful attention must be paid to haemodynamic stabilisation and optimising fluid balance. Co-existent bacterial sepsis is frequently present in patients with malarial ARDS should be tackled with an appropriate broad spectrum antibiotic therapy. There is pressing need of emergency medicine to manage critically ill patients. Cerebral malaria should always be suspected in a patient with altered sensorium in a malaria-endemic area. However, other causes of unconsciousness such as encephalitis, meningitis or hepatic coma should also be excluded. Present study also highlights the changing trend of complicated malaria from cerebral malaria to graver ARDS and ARF with high mortality. This study confirms

presence of severe and complicated falciparum malaria in western Maharashtra.

## REFERENCES


1. Dash A P, Valecha N, Anvikar AR and Kumar A. Malaria in India: Challenges and opportunities. *J. Biosci*. 2008;**33**(4):583–592.
2. World Health Organization. World malaria situation in 1992, *Weekly Epid Report* 1994;**69**:309–32.
3. World Health Organization. Severe falciparum malaria, *Trans Roy Soc Trop Med & Hyg* 2000;**94**: supplement 1.1–90.
4. Kochar D, Kumawat BL, Karan S, Kochar SK, Agarwal RP. Severe and complicated malaria in Bikaner (Rajasthan), western India. *Southeast Asian J Trop Med Public Health*. 1997;**28**(2):259–67.
5. Mishra SK, Mohanty S, Mohanty A, Das BS. Management of severe and complicated malaria. J Postgrad Med. 2006;**52**(4):281–7.
6. Mishra SK, Mohanty S, Satpathy SK, Mohapatra DN. Cerebral malaria in adults - a description of 526 cases admitted to Ispat General Hospital in Rourkela, India. *Ann Trop Med Parasitol*. 2007;**101**(3):187–93.
7. Kochar DK, Kochar SK, Agrawal RP, Sabir M, Nayak KC, Agrawal TD *et al*. The changing spectrum of severe falciparum malaria: a clinical study from Bikaner (northwest India). *J Vector Borne Dis*. 2006;**43**(3):104–8.
8. Jain V, Nagpal AC, Joel PK, Shukla M, Singh MP, Gupta RB *et al*. Burden of cerebral malaria in central India (2004-2007). *Am J Trop Med Hyg*. 2008;**79**(4):636–42.
9. Chishti SA, Duidang L, Kasar A, Raman M, Luikham A. Severe falciparum malarial complications in Ukhrul, Manipur. *Indian Med Assoc*. 2000;**98**(10):619–22.
10. Mohanty S, Mishra SK, Pati SS, Pattnaik J, Das BS. Complications and mortality patterns due to *Plasmodium falciparum* malaria in hospitalized adults and children, Rourkela, Orissa, India. *Trans R Soc Trop Med Hyg*. 2003;**97**(1):69–70.
11. Mishra SK, Mahanta KC, Mohanty S. Malaria associated acute renal failure--experience from Rourkela, eastern India. *J Indian Med Assoc*. 2008;**106**(10):640–2, 654.
12. Harris VK, Richard VS, Mathai E, Sitaram U, Kumar KV, Cherian AM *et al*. A study on clinical profile of falciparum malaria in a tertiary care hospital in south India. *Indian J Malariol*. 2001;**38**(1–2):19–24.
13. Prakash J, Singh AK, Kumar NS, Saxena RK. Acute renal failure in Plasmodium vivax malaria. *J Assoc Physicians India*. 2003;**51**:265–7.
14. Kanodia KV, Shah PR, Vanikar AV, Kasat P, Gumber M, Trivedi HL. Malaria induced acute renal failure: a single center experience. *Saudi J Kidney Dis Transpl*. 2010;**21**(6):1088–91.
15. Mehta KS, Halankar AR, Makwana PD, Torane PP, Satija PS, Shah VB. Severe acute renal failure in malaria. *J Postgrad Med*. 2001;**47**(1):24–6.
16. Maheshwari A, Singh AK, Sinha DK, Tripathi K, Prakash J. Spectrum of renal disease in malaria. *J Indian Med Assoc*. 2004;**102**(3):143, 146, 148 passim.
17. Krishnan A, Karnad DR. Severe falciparum malaria: an important cause of multiple organ failure in Indian intensive care unit patients. *Crit Care Med*. 2003;**31**(9):2278–84.