

Original Research Article

Clinical spectrum of severe *Plasmodium falciparum* malaria in a tertiary care centre of eastern India.

ABSTRACT

Introduction:

Plasmodium falciparum malaria is the major public health problem presented with varied clinical severity. This study was carried out to observe the clinical spectrum of severe *falciparum* malaria in a tertiary health care centre.

Methods:

This study was undertaken in hospitalized adults with suspected severe malaria. Confirmation of *falciparum* infection was done by ICT/QBC and single-step-PCR. Diagnosis of severe malaria was done by WHO- guideline 2010.

Results:

450 adult cases with *falciparum* infection were studied. Maximum number of cases was from 15-25 years age group depicting the high exposure to malaria. In these patients, acute renal failure (ARF) as most common (36.2%) complication followed by cerebral malaria (35.3%), jaundice (27.8%), hepatic dysfunction (21.8%), respiratory distress (18.4%), severe malarial anemia (15.8%), thrombocytopenia (15.1%), and hypoglycemia (9.3%). Mortality was found in 6.0% of cases. Cerebral involvement and ARF were the common cause of death in these patients.

Conclusion:

ARF is the most common type of clinical severity followed by cerebral malaria in adults and both are equally responsible for death along with other complications. Looking into the matter of varied clinical severity, accurate diagnosis, effective anti-malarial treatment along with supportive therapy is necessary to triumph over this deadly severe *falciparum* malaria.

7 *Keywords: Plasmodium falciparum; Severe Malaria; Cerebral Malaria; Anemia; Acute Renal*
8 *Failure; Mortality*

9

10 **1. INTRODUCTION**

11

12 *Plasmodium falciparum* malaria is one of the most important causes of death and
13 considered as a major global health concern. Regardless of many control strategies by
14 national and international communities, *falciparum* malaria contributes to high morbidity
15 and mortality amongst all the infectious diseases worldwide, accounting for 198 million
16 positive cases of malaria and 584,000 deaths [1]. In India, of the 1.2 billion people, 80%
17 live in malaria risk areas [2]. According to World Malaria Report, the number of cases of
18 malaria reported from the country was 881,730 [1]. The number of deaths due to malaria
19 is 8.75 times higher in subjects ≥ 5 years (42,000 deaths) compared to children < 5 years
20 (4,800 deaths) [3].

21 Management of severe malaria cases is going to be a challenge for treating
22 physician due to emergence of drug resistance parasites [4]. Various studies in adults
23 with severe *P. falciparum* malaria showed a changing spectrum in last two decades. The
24 clinical spectrum of severe *P. falciparum* varies with population and endemicity of malaria
25 [5]. Studies undertaken in different parts of India on spectrum of severe *P. falciparum*
26 malaria showed variation [4,6,7]. The present study was undertaken to define the
27 spectrum of severe *P. falciparum* malaria in adults in a tertiary care centre. Further, this
28 data will support for the better management of patients with severe *P. falciparum* malaria
29 in the study sites.

30

31 **2. MATERIALS AND METHODS**

32

33 This prospective cohort study was undertaken in Sickle Cell Clinic and Molecular
34 Biology Laboratory, Department of Medicine, Veer Surendra Sai Medical College, Burla
35 (now renamed as Veer Surendra Sai Institute of Medical Sciences and Research, Burla)
36 in the state of Odisha, eastern India. It is a tertiary care, referral hospital for 12 million

people residing in western Odisha and the state of Chhattisgarh. The state of Odisha is situated along the Bay of Bengal and extends from 17.78°N to 22.73°N latitude to 81.37°E to 87.53°E longitude. The study site is situated between the geographical co-ordinates of 21.50° N and 83.87° E. Malaria is the major public health problem in this geographical region. The state of Odisha is considered as a region for hyperendemic and low perennial transmission of malaria with a seasonal peak from July to October [8]. This state contributes to 23% of malaria positive cases, 50% of *P. falciparum* cases and 15% of malaria related deaths in India [9]. In the study area, *P. falciparum* alone accounted for 87.8% of malarial infections compared to 50% of *P. falciparum* infection in India [10].

2.1. Study subjects:

Patients aged ≥15 years with clinically suspected malarial infections, hospitalized in the Department of Medicine, Veer Surendra Sai Institute of Medical College Burla, between August, 2010 to December, 2014 were included in the study. All the cases were subjected to either immune chromatography test (SD, Bio Standard Diagnostics India) or Quantitative Buffy Coat (QBC) (BD, Becton Dickinson Diagnostics) followed by single step polymerase chain reaction in all cases for confirmation of *Plasmodium* species [11]. Severity of *P. falciparum* malaria was defined as per WHO criteria 2010 [12]. The most severe complication, cerebral malaria (CM) was defined as patients with any of the features like altered sensorium, convulsion or GCS (Glasgow Coma Score) of ≤ 10. Other complications like severe malaria anemia (SMA) (hemoglobin, < 5 g/dl), acute renal failure (ARF) (serum creatinine > 3 mg/dl), *jaundice* (serum bilirubin >3 mg/dl), hepatic dysfunction (alanine transaminase (ALT)/ aspartate transaminase (AST) > 3 times of normal), respiratory distress, hemoglobinuria (dark red or black colored urine positive for hemoglobin), thrombocytopenia (platelet count <50,000/μL) and shock (systolic BP of < 80 mm Hg) were considered. Written informed consent was obtained from all the cases. This study was approved by institutional ethical committee of Veer Surendra Sai Medical College, Burla.

64 **2.2. Exclusion criteria:**

65 The following cases were excluded from the study (a) subjects co-infected with other
66 *Plasmodium* species; (b) children <15 years of age; (c) subjects having chronic disease
67 like tuberculosis, chronic renal failure, cirrhosis of liver and autoimmune diseases like
68 systemic lupus erythematosus and rheumatoid arthritis; (d) patients with dengue fever; (e)
69 pregnant women; (f) patients positive for hepatitis; (g) subjects who refused to consent for
70 the study.

71 **2.3. Laboratory Investigations:**

72 *P. falciparum* examination was made by either ICT or QBC and single step PCR. All
73 the subjects were screened for sickle cell by sickling slide test. Those found positive were
74 subjected to agarose gel Hb electrophoresis (pH 8.6). A complete blood count was done
75 on an automated hematology analyzer (Sysmex pocH-100i; Sysmex Corporation, Kobe,
76 Japan). Biochemical parameters such as serum bilirubin, creatinine, urea, alanine
77 transaminase, aspartate transaminase, sodium, potassium, glucose were done in a semi
78 auto-analyzer (Erba Chem 7; Erba Diagnostics Mannheim GmbH, Mannheim, Germany)
79 as per the manufacturer's instructions.

80 **2.4. Molecular confirmation of *P. falciparum*:**

81 The molecular confirmation of *P. falciparum* was done by method described earlier
82 [11]. Briefly, three primers namely PL3, PL4 and PL5 specific to the *P. falciparum* and *P.*
83 *vivax* were used for confirmation of *Plasmodium* species. PL3 (5'-
84 ATGGCCGTTTTAGTTCGTG-3') and PL4 (5'- GGAAACGGTACGATAAGCCA-3')
85 amplified a 346 bp product specific for *P. faciparum* where as PL3 (5'-
86 ATGGCCGTTTTAGTTCGTG-3') and PL5 (5'- ACGCGTGCAGCCTAGTTTAT-3')
87 amplified a 266 bp product specific for *P. vivax*. A 25µL of PCR reaction mixture contain
88 200ng of genomic DNA, 2.5µL of primer PL3 (10 picomole), 2 µL of each primer PL4 (10
89 picomole) and PL5 (10 picomole), 2.5µL of 10x PCR buffer, 2.5µL of 25mM MgCl₂ 0.5
90 units of DNA Taq polymerase (Merck Biosciences Pvt. Ltd.). The PCR reaction mixture

91 was heated initially at 94°C for 4 minutes and was kept for 30 cycles each of denaturation
 92 at 94°C for 30 seconds, annealing at 54°C for 30 seconds and extension at 72°C for 30
 93 seconds followed by final extension at 72°C for 5 minutes. The PCR amplified gene
 94 fragments were electrophoresed on 2% agarose gel, and visualized under Gel
 95 documentation system (Model: GelDoc XR; Make: BioRad Laboratories, USA) after
 96 ethidium bromide staining. This allowed the presence of *P. falciparum* or *P. vivax* by size
 97 of PCR product.

98 **2.5. Statistical Analysis:** Statistical analysis was done using Graph Pad Instat,
 99 window 3.00. $p < 0.05$ was considered statistically significant.

100 **3. RESULTS:**

101 During the study period, 531 cases had suspected malarial infections. Of which, 377
 102 (71.0%) were found positive either by ICT or QBC and 450 (84.7%) cases were positive
 103 for single step PCR. The entire lot of cases positive for ICT/QBC was found to be positive
 104 for single step PCR. Finally, 450 patients were included in the study. The mean age of the
 105 patients was 34.4±13.5 years (range, age 15 to 65 years) and majority were males (315,
 106 70.0%).

107 CBC parameters showed 10.2 % (46/450), 14.6% (66/450), 42.9% (193/450) and
 108 31.8% (143/450) of patients had hemoglobin level <5 mg/dL, ≥ 5 to < 7 mg/dL, ≥ 7 to < 10
 109 mg/dL and ≥ 10 mg/dL respectively. Individual data for red cell indices explained 43.1% of
 110 patients had microcytic (<76fL of MCV) and hypochromic (<27 pg of MCH) blood picture.
 111 The hematological and biochemical parameter have been presented in Table 1.

112 The patients under this study were divided into 5 groups on the basis of increasing
 113 age [Table 2]. The majority (151, 33.6%) of patients belonged to 15-25 years age group
 114 and minimum (40, 8.9%) were from >55 years age group. There was no difference in the
 115 sex distribution in five age groups (χ^2 , 0.226; $p = 0.63$). Screening of sickle cell resulted
 116 30 patients with sickle cell trait (HbAS) and 14 patients with sickle cell anemia (HbSS).

117 Majority of patients with sickle cell anemia and severe *falciparum* malaria were from 15 to
118 35 years of age [Table 2].

119 Clinical finding of the hospitalized patients showed fever in all the patients, where as
120 vomiting, pallor and headache were present in 32.7%, 32.0% and 21.0% respectively.
121 Shock was observed in 15 (3.3%) of patients. Majority of our cases had ARF in 36.2%
122 followed by CM (35.3%), jaundice (27.8%), hepatic dysfunction (21.6%), respiratory
123 distress (18.4%), thrombocytopenia (15.1%), SMA (10.2%) and hypoglycemia (9.3%).
124 The detailed clinical parameters are depicted in Figure 1.

125 On comparison of age distribution of major clinical signs and symptoms the following
126 were found. The incidence of SMA was highest (15.0%) in patients with age > 55 years.
127 ARF was common in patients > 36 years of age. Hypoglycemia was in decreasing order
128 with increasing age. Incidence of jaundice was high in patients with 36-45 years of age.
129 CM was highest in patients with > 55 years of age group followed by 16-36 years age
130 group and 36-55 years of age group. All other parameters were comparable in each age
131 group. The incidence of major clinical signs and symptoms defining severe malaria in
132 different age groups was depicted in figure 2. Out of 14 patients with malaria and sickle
133 cell anemia, the incidence of CM, SMA and ARF 5 had SMA, 4 had CM, 6 had painful
134 crises with SMA, 2 had ARF and only one patient associated with both hepatic
135 dysfunction and painful crises.

136 Severe malaria has been defined on the basis of presence of various complications.
137 In this study, the severe malaria has been defined by presence of single complication in
138 194 patients and more than one complication in 256 patients (two complications in 173
139 patients, three complications in 58 patients, four complications in 18 patients and five
140 complications in 7 patients). Among the patients with multiple complications, 14.8%
141 (38/256) patients had ARF with hepatic dysfunction followed by CM with ARF (5.9%,
142 15/256).

143 Death has been recorded in 27 (6.0%) patients in this study. The cause of death in
144 different age groups has been illustrated in Table 3. Majority of patients were in 15-25
145 years of age group (44.4%, 12/27). Amongst the death patients, CM and ARF were the
146 two important cause for death in 19 patients each (70.4%). Three patients with sickle cell
147 anemia had died.

148 **4. DISCUSSION:**

149 In this prospective hospital based study, we have included 450 patients with severe
150 *P. falciparum* malaria. The mean age of the patients was 34.4±13.5 year with majority
151 (70.0%) being males. Of all the cases positive for single step PCR, 83.8% (377/450) of
152 cases were found positive for *P. falciparum* by either ICT or QBC; resulting in 16.2% of
153 more accuracy in PCR based detection of *P. falciparum*.

154 The sizable number of adults included in this study with severe malaria could be due
155 to lack of premunition because of low and markedly seasonal transmission of malaria in
156 this area. Another possibility could be due to concentration severe cases being referred to
157 this hospital for availing tertiary care facilities. Along with normal hemoglobin genotype
158 (HbAA), we have found 30 patients with sickle cell trait and 14 patients with sickle cell
159 anemia.

160 In this study we have found 15-25 years age group were more vulnerable to severe
161 malaria and required hospitalization followed by 26-35 years of age group. Recently
162 similar observations have been reported in two different studies from India [6,13]. In last
163 two decades, the spectrum of severe malaria have been changed significantly [14]. Along
164 with CM and SMA, other factors like jaundice, ARF and hepatic dysfunction are now
165 contributing to malarial mortality. Studies on the spectrum of severity are necessary for
166 better understanding of the dynamics of infection complexity and immune interaction in
167 adults [15]. In the present study, fever along with ARF was the commonest clinical
168 presentation followed by CM. The emergence of ARF as an important clinical
169 manifestation of severe *P. falciparum* malaria in adults has also been described in earlier

170 studies from Vietnam and from different parts of India [13,14,16]. Several hypotheses
171 such as mechanical obstruction by infected erythrocytes, immune mediated glomerular
172 and tubular pathology, fluid loss due to multiple mechanisms and alterations in the renal
173 microcirculation, etc, have been proposed as causative mechanism of ARF. In severe
174 malaria cases usually ARF is associated with other complications [17]. In our study of 163
175 cases with ARF, CM was found in 49 cases, hepatic dysfunction in 62 cases, SMA in 14
176 cases, thrombocytopenia in 18 cases and respiratory distress in 16 cases.

177 SMA is the cause of fatal outcome in children rather than in adults [18]. Severe
178 malaria with reduced level of hemoglobin (<5 mg/dL) was observed in 46 (10.2%) cases
179 in our study. It has been suggested that *P. falciparum* glycosylphosphatidylinositol toxin
180 interacts with the non parasitized red cells membrane contributing to malarial anemia
181 [19]. The incidence of anemia in our patients is higher compared to 7.7% reported by Das
182 LK et al, [4]. whereas lower compared to two studies in India [6,20]. The lower incidence
183 of anemia with microcytic red cells in our patients might be due to presence of alpha
184 thalassemia, a malaria protective hemoglobin disorder highly prevalent in study area [21].

185 Hepatic dysfunction characterized by increased level of liver enzymes was noticed in
186 21.6% of cases. This incidence was comparable in all age groups. Hepatic dysfunction
187 occurs mainly due to sequestration of parasite infected red cells in the liver capillaries
188 resulting ischemia [22]. In this study we have observed that along with the raised liver
189 enzymes value, 79.4% of cases had raised bilirubin level (>2 mg/dL), while the incidence
190 of jaundice alone without raised level of liver enzymes was 27.8% depicting the invasion
191 of red cells by *P. falciparum* resulting hemolysis and increased bilirubin level. The
192 incidences of jaundice in adults in other parts of India were 15.0% [6] and 18.8% [7]
193 which were low comparable to our data. Asma et al, [6] and Croft AM et al, [23] have
194 proposed the possible role of anti-malarial drug toxicity as an underlying contributing
195 factor for causing damage to hepatocytes and leakage of enzymes.

196 The other major clinical feature observed in this study was hypoglycemia in 42
197 (9.3%) cases. This finding is in accordance with 8.0 % incidence of hypoglycemia in
198 South-East Asian adults [24]. Hypoglycemia was associated with CM (11, 26.2 %), ARF
199 (11, 26.2 %), Jaundice (9, 21.4 %) and SMA (5, 11.9 %) in our study. Hypoglycemia in
200 *falciparum* malaria is usually ascribed to increased glucose use and impaired glucose
201 production caused by the inhibition of gluconeogenesis. It has been reported that patients
202 with prolonged fasting usually had hypoglycemia [25]. Though we have not investigated
203 the duration of fasting in these patients during infection period, this might be a factor.

204 In severe *P. falciparum* malaria, respiratory distress develops in 25.0 % of adults
205 due to respiratory compensation of metabolic acidosis, noncardiogenic pulmonary
206 edema, concomitant pneumonia, and severe anemia [26]. In our study 18.4% of cases
207 had respiratory distress with majority in the 46-55 years age group. Recently similar
208 observation has been reported on eHealthMe study from FDA and social media reports
209 [27]. It stated the incidence of respiratory distress is high in male compared to female
210 which is opposite to ours; we found this in 17.8% of males and 22.4% of females.

211 Severe malaria is associated with thrombocytopenia. The various mechanism
212 causing thrombocytopenia are coagulation disturbances, splenomegaly, bone marrow
213 alterations, antibody mediated platelet destruction, oxidative stress etc. [28]. Many
214 studies have reported the high incidence of thrombocytopenia with *P. falciparum* malaria.
215 In our study, the incidence of thrombocytopenia was 15.1% which is very low compared
216 to earlier studies [6,28-30,31]. Recently, in a multi institutional study thrombocytopenia
217 was defined as a marker of disease severity and has a low prognostic utility, triage and
218 management in adults with *falciparum* malaria [31].

219 Fourteen patients had *P. falciparum* malaria with sickle cell anemia presented with
220 multiple clinical symptoms. The commonest symptom was vaso-occlusive crises (8/14)
221 followed by jaundice (6/14), hepatic dysfunction (5/14), CM (4/14), SMA (4/14), ARF
222 (3/14) and respiratory distress (2/14). The mean hemoglobin level was 7.6 mg/dL, ranging

from 3.4 mg/dL to 10.9 mg/dL. During hospitalization 3 patients required blood transfusion. Surprisingly along with sickle cell anemia, we have registered 30 patients (6.7%) with sickle cell trait in severe *P. falciparum* malaria. The common causes of severity in these patients were CM and ARF. It has been hypothesized that, sickle cell trait protects against severity of disease due to *P. falciparum* malaria [32]. The finding of severe malaria with sickle cell trait in this region could be due to two reason (1) the prevalent of sickle cell gene in the study area was found to be 21% [33]. (2) negative epistatic interaction between sickle cell trait and alpha thalassemia on *P. falciparum* malaria [34]. Though we have not analyzed the presence of alpha thalassemia in our patients, the prevalence of this inherited hemoglobin disorders in the study area is approximately 50% [21]. The presence of microcytic red cells picture in 41.3% of our patients also corroborated the presence of alpha thalassemia.

We have recorded 27 (6.0%) deaths in this study. Both CM and ARF are major clinical complications responsible for death. In 22 (81.5%) of the cases, two or more complications were present indicating poorer prognosis as the number of complications increases. The highest percentage (10.0%, 4/40) of death was found in patients with > 55 years of age followed by 15-25 years of age group (7.9%, 12/151). This might be due to reduced immune mediated resistance against malarial infection in older age. The later might be due to over exposure to malaria infection. There were three deaths among patients with sickle cell anemia (21.4%; 3/14). All the three patients had repeated episodes of vaso-occlusive crises. Other causes responsible for death in these patients are CM and SMA. There were no studies describing the association of sickle cell anemia and malaria in India. Studies from Africa have represented that, though the protection afforded by sickle cell anemia is high compared to sickle cell trait, malaria is an important cause of death in patients with sickle cell anemia when affected [35,36].

We have certain limitations in this study. (1) We have not analyzed the effect of parasitemia with the clinical severity of malaria. (2) We have not recorded the number of

cases diagnosed by either ICT or QBC separately in the initial screening procedure for *P. falciparum* infection, because the decision for diagnosis for *P. falciparum* infection by either ICT or QBC is depended upon treating physicians, so we have considered both the tests for infection.

5. CONCLUSION:

The clinical severities of *P. falciparum* malaria may vary and depend upon the age of the patients, malaria endemicity, and transmission pattern. Of the various complications determining severity due to *P. falciparum* infection, CM and ARF were the two important factors responsible for fatality in these patients. It is important to prevent the exposure of malaria in adults in the age group of 15-25 years who are found to be most vulnerable for malarial infection. Along with early and appropriate anti-malarial drugs, exact diagnosis and management of complications are necessary to overcome the disease severity in a malaria endemic region.

CONSENT

Written informed consent was obtained from the patients (or from the guardian in case of minor). In case of unconscious patients, the consent has been obtained from patient's relative.

ETHICAL APPROVAL

This study was approved by Institutional Ethical Committee of Veer Surendra Sai Institute of Medical Sciences and Research, Burla.

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367

368 **Table-1.** Hematological and biochemical parameters of severe *P. falciparum* malaria cases
369 (n=450).

370

Parameters	Mean $\pm$ SD	Minimum	Maximum
Hemoglobin (g/dL)	8.9 $\pm$ 3.0	2.1	23.9
White Blood Cells ($\times 10^3/\mu\text{L}$)	8.8 $\pm$ 4.17	1.6	38.6
Red Blood Cells ($\times 10^6/\mu\text{L}$)	3.68 $\pm$ 1.22	0.71	8.9
Mean Corpuscular Volume (fL)	78.3 $\pm$ 10.0	43	120
Mean Corpuscular Hematocrit (pg)	26.0 $\pm$ 3.6	10.9	36.8
Mean Corpuscular Hemoglobin Concentration (g/dL)	32.2 $\pm$ 2.5	19.4	40
Platelets ($\times 10^3/\mu\text{L}$)	162.7 $\pm$ 99.7	10	917
Lymphocytes (%)	27.3 $\pm$ 13.3	3.7	73
Monocytes (%)	11.7 $\pm$ 8.2	2.1	39.7
Neutrophil (%)	66.6 $\pm$ 14.2	20	93
Glucose (U/L)	115.1 $\pm$ 54.0	28	592
Serum Urea (mg/dL)	65.4 $\pm$ 59.6	10	427

Serum Creatinine (mg/dL)	2.82±2.91	0.2	19.5
Serum Bilirubin (mg/dL)	3.47±4.7	0.07	54.3
Serum Aspartate Transaminase (AST) (mg/dL)	90.0±127.0	2.3	1524
Serum Alanine Transaminase (ALT) (mg/dL)	75.8±104.5	5.4	1307
Sodium (U/L)	132.9±7.9	96.4	171
Potassium (U/L)	4.22±1.2	2	6

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374 **Table-2.** Age and gender wise distribution of severe *P. falciparum* malaria cases with sickle

375 cell gene status.

Age groups	Total No. of cases	Male	Female	Sickle Cell Trait (HbAS)	Sickle cell anemia (HbSS)
(in years)	Number (%)	Number	Number	Number	Number
15-25	151 (33.6%)	105	46	10	6
26-35	114 (25.3%)	78	36	6	6
36-45	89 (19.8%)	63	26	6	0
46-55	56 (12.4%)	40	16	5	1
>55	40 (8.9%)	29	11	3	1
Total cases	450	315	135	30	14

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378 **Table-3.** Number and cause of death in different age groups of severe *P falciparum* malaria

379 cases (n=450).

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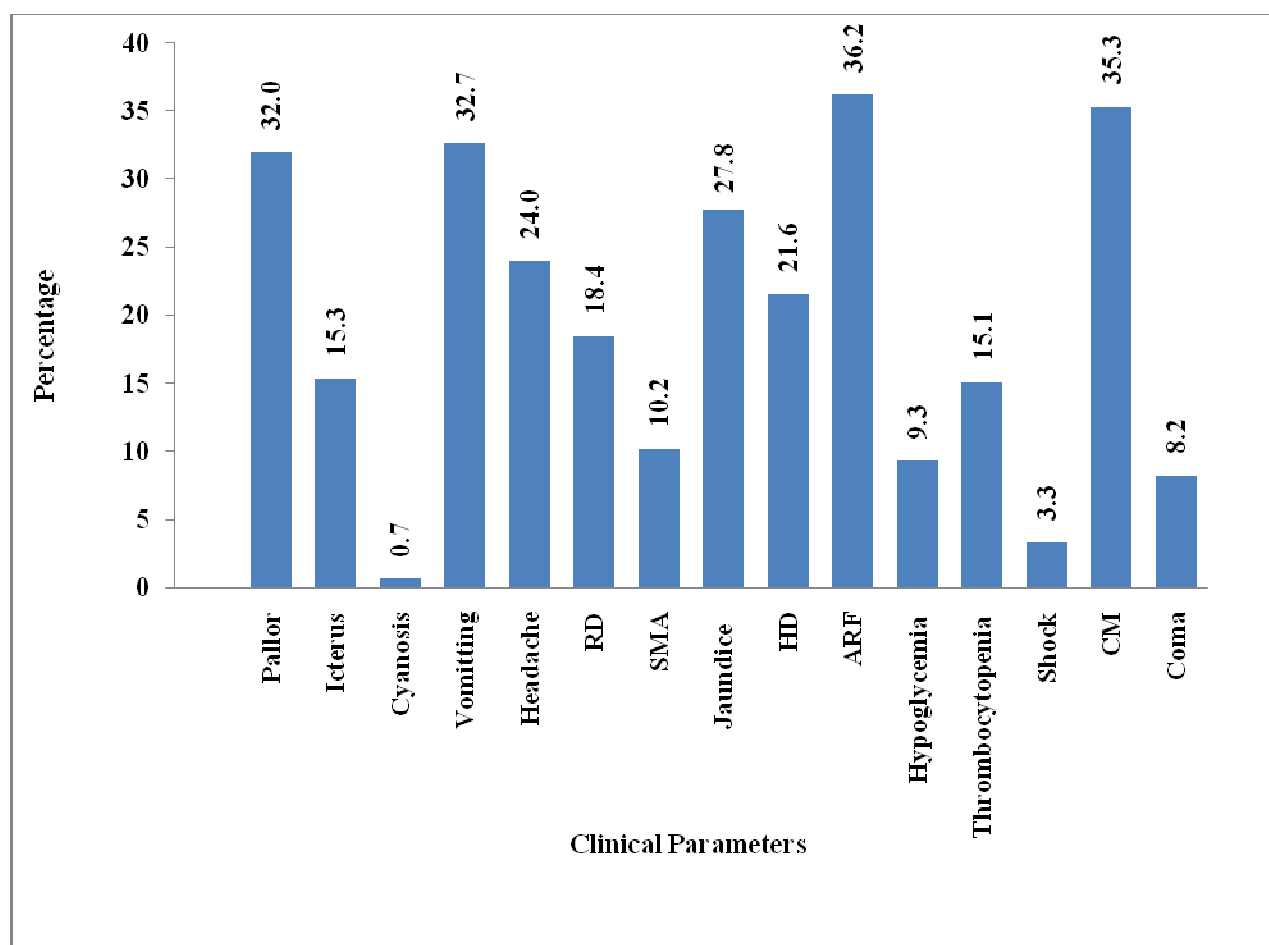
Age Groups (In years)	Total no of patients (No.)	Death (No., %)	Cause of death	No of cases
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15-25	151	12 (7.9%)	1. CM+ARF+HD+RD	1
			2. CM+ARF+HD	1
			3. CM+ARF	2
			4. CM+ARF+SMA+T	1
			5. CM+RD (SCA)	2
			6. CM+J+RD+SMA (SCA)	1
			7. ARF+HD+SMA (SCA)	1
			8. ARF+HD	1
			9. ARF	1
			10. CM	1
26-35	114	5 (4.4%)	1. CM+ARF+HD+SMA+T	1
			2. CM+ARF+HD	1
			3. CM+ARF+SMA	1
			4. CM+HYPO	1
			5. ARF	1
36-45	89	3 (3.4%)	1. CM+ARF+HD+SMA	1
			2. CM+ARF	1
			3. ARF+HD+SMA	1
46-55	56	3 (5.4%)	1. CM+ARF+HD+SMA	1
			2. CM+HYPO+SMA	1
			3. ARF	1
>55	40	4 (10.0%)	1. CM	1
			2. CM+J+RD+SMA	1
			3. CM+ARF+J	1
			4. ARF+RD+T	1
Total number of cases				27

381 **Note:** CM, Cerebral Malaria; ARF, Acute Renal Failure; SMA, Severe Malarial Anemia; HD,
382 Hepatic Dysfunction; RD, Respiratory Distress; J, Jaundice; HYPO, Hypoglycemia; T,
383 Thrombocytopenia; SCA, Sick Cell Anemia.

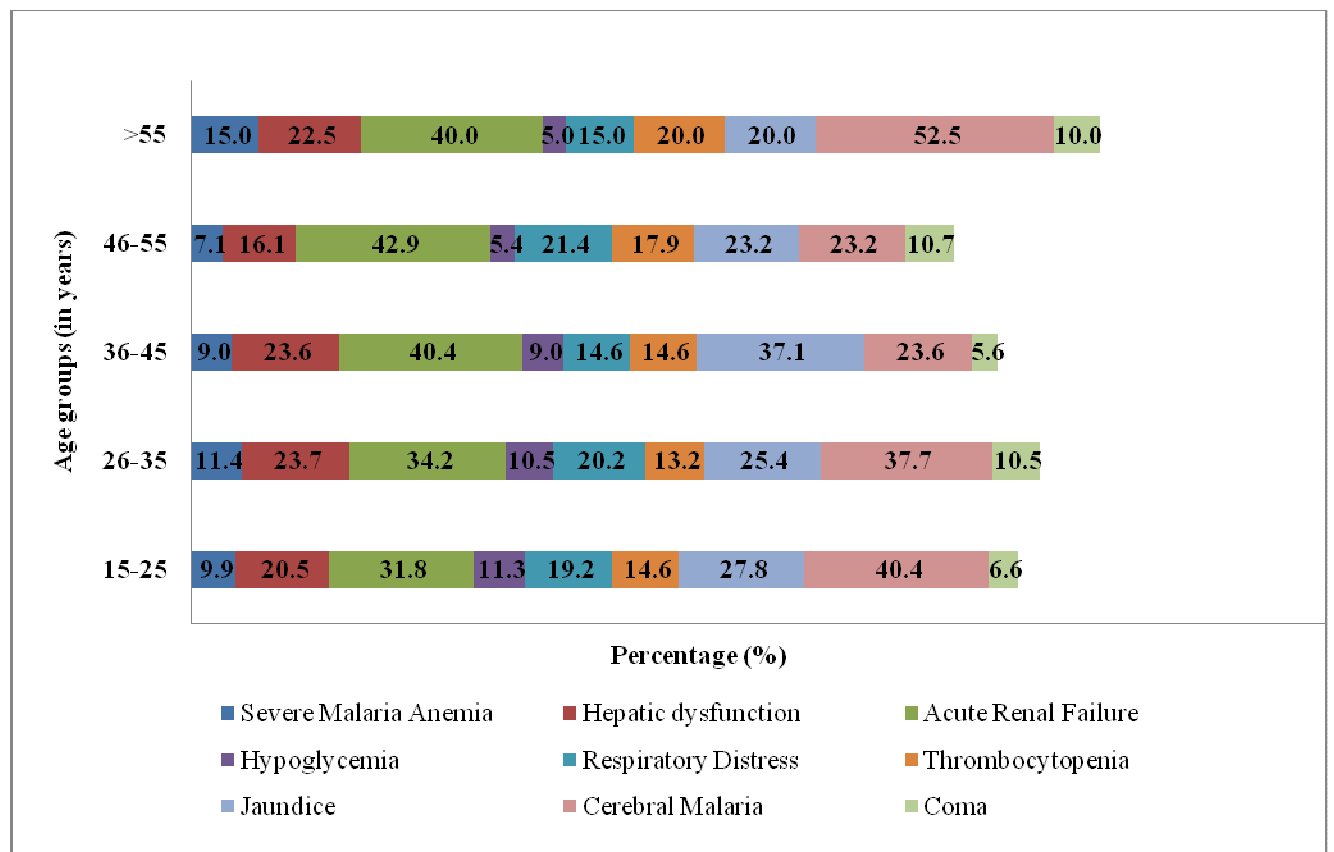
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394 **Figure 1.** Incidence of different clinical parameters in severe *P falciparum* malaria cases
395 (n=450).



Note: RD, Respiratory Distress; SMA, severe malarial anemia, HD, Hepatic Dysfunction;
ARF, Acute Renal Failure; CM, Cerebral Malaria

Figure 2. Incidence of different clinical parameters in different age groups of severe *P. falciparum* malaria cases (n=450).



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