International Journal of Advances in Medicine
Choudhary H et al. Int J Adv Med. 2017 Dec;4(6):1591-1598
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20175173

Original Research Article

Study of clinical presentation of falciparum malaria and correlation with laboratory indices of poor prognosis

Hazarimal Choudhary[1], Prema Ram Choudhary[2]*

[1]Department of Medicine, Bangor Government Hospital, Pali, Rajasthan, India
[2]Department of Physiology, C. U. Shah Medical College, Surendranagar, Gujarat, India

Received: 18 August 2017
Accepted: 19 September 2017

***Correspondence:**
Dr. Prema Ram Choudhary,
E-mail: prema5252@gmail.com

ABSTRACT

Background: Severe malaria is a chief cause of death in the North-eastern states of India. The criteria for defining severe malaria have fluctuating over the last many years. Detection of both specific and sensitive clinical features of falciparum malaria to predict death is required to improve clinical management. Therefore, the objective of present study was designed to investigate the clinical presentation of falciparum malaria and correlation with laboratory indices of poor prognosis.
Methods: This prospective observational study was conducted at the R N T Medical College Udaipur, India. Total 53 malarial patients who tested positive for plasmodium falciparum were included. A detailed clinical presentation, haematological and biochemical variables were scrutinized. SPSS-16 software was used for statistical analysis.
Results: Out of 53 patients, 6 (11.3%) patients had (>5%) parasitaemia, 3 (5.66%) patients had schizonts in peripheral blood film, 2 (3.77%) patients had serum creatinine >3.0 mg%, 4 (7.54%) patients had raised SGOT and SGPT and all have been died while 11 (20.75%) patients had haemoglobin <7.1 gm% and amongst these 3 (27.27%) patients were died. Out of 53 patients, 13 patients (24.53%) died. Most of the patients had over lapping features with anemia (13.32%), ARDS, 16.98 %, Jaundice 9.43% and impaired consciousness (32.96%). These four features were responsible for high incidence of mortality in malaria.
Conclusions: Decisively 29 (54.71%) patients were having laboratory indices of poor prognosis and amongst them 19 (65.51%) patients were died. Therefore, our findings confirm that patients who had P. falciparum malaria with laboratory indices of poor prognosis had high incidence of mortality.

Keywords: ARDS, Clinical presentation, Malaria, Plasmodium falciparum, Poor prognosis, Severe malaria

INTRODUCTION

Malaria is a foremost communal health trouble in India as well as several parts of the globe. According to world malaria statement 2013 there were 207 million cases of malaria in 2012 consequential in 627000 deaths. Thirteen percent of these cases were accounted from South East Asia, 52% of which were reported from India. India contributed 1.04 million of malaria cases leading to 504 deaths.[1] Malaria is a potentially life-threatening parasitic disease caused by Plasmodium species such as *Plasmodium vivax, Plasmodium falciparum, Plasmodium malariae and Plasmodium ovule*.[2] In India about 70 % of infection is reported to be due to *Plasmodium vivax*, 25-30% *Plasmodium falciparum*, 4-8% mixed infection and less than 1 % due to *Plasmodium malariae*. *Plasmodium ovale* has not yet been reported from India; it is generally confined to Tropical Africa and has also been reported in Vietnam.[3] The occurrence of *P. falciparum* in India is rising. The whole population of India (99.5%) is nowadays deemed to be under malaria jeopardy.[4] Although in majority of cases, malaria presents as a

straightforward fever with punctual recovery, it may present in severe appearance with systemic complications particularly renal and hepatic failure, leading to high morbidity and mortality.[1,5] More recently, *Plasmodium falciparum* accounts for nearly 50% of reported malaria cases in India. The major endemic areas in India are in the Northeastern states and Mewar region of Rajasthan. The clinical manifestation of *P. falciparum* infection are caused by the asexual blood stages and can lead to cerebral malaria, anemia, acute renal failure, jaundice, hematuria, acute malarial hepatitis, shock, disseminated intravascular coagulation (DIC), hypoglycemia, hyperpyrexia, non-cardiogenic pulmonary edema, adult respiratory distress syndrome (ARDS), adrenal insufficiency-like syndrome, hyper-parasitemia, black-water fever, cardiac arrhythmias, and gastrointestinal syndromes.[6-8] Classically, an elevated parasite count is related with a more severe infection and increased mortality.[9,10] The high mortality rate from *P. falciparum* is due to its aptitude to induce severe malaria, and in some cases, multiple organ dysfunction. The presenting symptoms and mortality patterns of severe malaria differ extensively according to the geographical setting and transmission strength.[2] Literatures from India describing the clinical presentation and scream are scanty and insufficient due to numerous reasons like non-availability of diagnostic facility, deficient malarial worker or technician at primary health care centre, lack of appropriate system of reporting, and lack of will power among the health care professionals to build-up a database.[11] In addition, various earlier studies related to epidemiology and clinical manifestations have shown a lot of discrepancies.[12-14] Therefore the present study was undertaken to clinical presentation of falciparum malaria and correlation with laboratory indices of poor prognosis in population of Mewar region of Rajasthan, India.

METHODS

Study design and participants

This prospective observational study was conducted at the department of general Medicine, R N T Medical College Udaipur, India. All falciparum malarial patients, either sex, aged between 10-70 years, were selected from the cases admitted in Department of general Medicine, R N T Medical College and associate hospital. Total 53 malarial patients mean age 40.53±4.60, who tested positive for plasmodium falciparum (peripheral blood smear positive and rapid diagnostic antigen detection test positive) were included in the present study. Patients with history of malignancy, alcoholics, congestive cardiac failure, pregnant women and liver disease were excluded from study. They were also excluded if patients having other co-infection (i.e. enteric fever, dengue fever, sepsis, urinary tract infection, HIV/HBsAg positive patients, meningitis and encephalitis) that interferes the clinical presentation of P. falciparum malaria. After establishing the diagnosis of malaria, trained interviewers, using a structured questionnaire, interviewed the all patients to obtain the information on socio-demographic characteristics, smoking, alcohol drinking habits, dietary characteristics, personal and family history of diseases and hospitalization. A complete clinical history was taken about the presence of fever, nausea, vomiting, pain abdomen, diarrhea, headache, delirium, convulsion, unconsciousness, aphasia, any neurological deficit, jaundice, yellow urine and anorexia. In addition, a complete clinical examination with special emphasis on fever, jaundice, and presence of hepatomegaly and splenomegaly, postural hypotension and complete neurological examination were performed using appropriate tool and technique. Informed written consent was obtained from all the patients or relative (guardian) prior to start the study. The study protocol was approved by institutional ethics committee.

Clinical assessment

The clinical studies of severe malaria, uncomplicated malaria and various atypical presentation of P. falciparum malaria were carried out. Severity and prognosis of falciparum was assessed by clinical and laboratory parameters as proposed by working group of World Health Organization.[15] Febrile patients with a positive Plasmodium falciparum histidine rich protein-2 (HRP2) based rapid test for falciparum malaria were entitled for a clinical evaluation of severe malaria, which included at least one of the subsequent conditions: cerebral malaria, Unarousable coma not attributable to any other reason, defined by a Glasgow Coma Scale (GSC) score <9. Coma should persist for at least 30 min after a generalized convulsion (convulsions with duration longer than 30 minutes or a frequency of 2 or more in the 24 hours preceding admission); severe symptomatic anemia, defined as severe pallor pooled with respiratory distress and hematocrit value <15% or hemoglobin concentration <50 gms/dL in the existence of parasite count >10 000/µl; Renal failure, defined as urine output <400 ml/24 hours in adults (<12 ml/kg/24 hours in children) and a serum creatinine >265 µmol/L (>3.0 mg/dl) despite adequate volume repletion; Pulmonary edema and acute respiratory distress syndrome (ARDS), defined as nasal alar flaring, costal indrawing, or use of accessory muscles, severe tachypnea, or deep breathing. In addition, the acute lung injury score is calculated on the basis of radiographic densities, severity of hypoxemia, and positive end-expiratory pressure; Hypoglycemia, defined as whole blood glucose concentration < 2.2 mmol/L (<40 mg/dl) or clinical perfection in the level of consciousness instantly after administration of 10% dextrose; circulatory collapse (algid malaria), defined as systolic blood pressure <70 mmHg in patients >5 years of age, with cold clammy skin or a core-skin temperature difference >10°C; Abnormal bleeding or disseminated intravascular coagulation (DIC), defined as spontaneous bleeding from gums, nose, gastrointestinal tract, or laboratory evidence of disseminated intravascular coagulation; Acidemia/acidosis, defined as arterial blood pH <7.25 or acidosis (plasma bicarbonate <15 mmol/l); Macroscopic

hemoglobinuria, defined as presence of red blood cells or hemoglobin in urine and hemolysis not secondary to glucose-6-phosphate dehydrogenase deficiency (G-6PD); prostration, defined as the incapability to sit unsupported (for children >6 months of age) or the failure to drink or breast-feed in younger children; Hyperparasitemia, defined as (asexual parasitemia) >5% parasitized erythrocytes or >250000 parasites/µL; Hyperpyrexia, defined as Core body temperature >40°C; Hyperbilirubinemia, defined as serum total bilirubin level >43 µmol/l (>2.5 mg/dl).[15,16] Furthermore, uncomplicated malaria was defined as a clinical malaria case: symptoms such as fever >38°C, headache, chills and/or malaise and a positive thick blood smear without severity criteria, despite of parasite species.[17]

Definition of laboratory indices for poor prognosis

The laboratory indices of poor prognosis of P. falciparum malaria was established according to The World health organization (WHO) criteria and it suggest that the following laboratory indices should be considered as indicative of poor prognosis in falciparum malaria: high parasitaemia with >5% (2,50,000 parasites/µL blood); existence of schizonts in peripheral blood film; peripheral leucocytosis, WBC>12,000411;high serum tumor necrosis factor alpha (TNF-α); haematocrit value <20% (Hb<7.1gm/dL); blood glucose <2.2mmo1/1 (<40 mg/dl);serum creatinine>265µmo1/1 (>3.0mg/dl); raised serum amino transferee (AST/ALT).[18]

Hematological parameters

Blood samples were achieved from all malarial patients by vein-puncture at the time of conscription and before the anti-malarial treatment. Samples were collected into K3-EDTA and blood clot activator test tubes were analyzed for hematological and biochemical parameters, respectively. Clot activator samples were immediately centrifuged (4000 rpm) for 10 minutes; the sera were separated and frozen at 10º C until analysis. Following laboratory investigations were performed to assess severity and prognosis of *P. falciparum* malaria. Hematological parameters total white blood cells (WBC) count and hemoglobin estimation were assessed using an automated hematological analyzer (Sysmex KX-21 N-3 Parts, Japan) as per recommended setting and calibration for human hematology were applied according to the manufacture's operation manual. Bleeding disorders markers; bleeding time (BT) and clotting time (CT) were deliberated using a Duke's and White methods, respectively.

Diagnosis of P. falciparum malaria and severity

Plasmodium falciparum malaria was diagnosed using a peripheral blood film examination and further conformed by commercially available rapid diagnostic malaria antigen test which detect *P. falciparum* histidine rich protein 2 (HRP2) or plasmodium specific lactate dehydrogenase (pLDH). (Combo Malaria Ag-pLDH/HRP2, PMC, Ltd Mumbai, India; was used for differential diagnosis of plasmodium species).

Level of parasitaemia was recognized by peripheral blood film. Thick and thin blood smears were stained using the field and JSB stain (Jaswant Singh and Bhattacharya stain). Smears were examined for presence of malaria parasite under oil immersion in at least 100 fields for less than 5 minutes. Parasite index (PI) was given the counting the numbers of parasites/100 RBC in thin smear. In case of thick smear parasite index counted by noting the number of parasite/200 WBC counted, multiplied by WBC count.[1] A count of one lakh parasites/ micro liter corresponds to 2 % parasitemia and a count of 2.5 lakh sparasites/µL is taken as 5% parasite index. The degree of parasitemia, which is parasitic index, was graded as less than 2%, between 2 to 5%, between 5 to 10% and more than 10%.[19-21]

Biochemical parameters

Sera were used for determination of biochemical parameters, at 37ºC by enzymatic method using commercial available diagnostic kit on fully automated biochemical analyzer. The parameters and the respectively methods applied are the followings: aspartate amino-transferase (AST) and alanine amino-transferase (ALT) - Henry method (Modified IFCC); Blood Urea-Urease method; random blood glucose-GOD/POD method; total serum bilirubin-Diazo method; serum creatinine-enzymatic method.

Others examination

Urine test strip (Biochemical examination of urine) and urine microscopic (for haematuria and haemoglobinuria) analysis were performed by urine complete examination. At time of recruitment, the axillary body temperature was measured with a digital thermometer, and the respiratory rate was recorded in structured proforma. Blood pressure was measured using a digital sphygmomanometer. Visceral examination of all patients was also carried out using an ultrasonography (USG) in the department of radiology.

Statistical Analysis

The data were statistically analyzed and baseline characteristics of the malaria patients were expressed in percentages. Chi-square test was used for the relationship of qualitative data. P< 0.05 was considered statistically significant. Statistical analysis was done using SPSS windows version 16.0 software (SPSS Inc., Chicago, Illinois).

RESULTS

The present study was performed on 53 *P. falciparum* malaria patients in Department of general Medicine, R N

T Medical College attached Maharana Bhupal hospital, Udaipur (Rajasthan) and the following outcomes were drawn from the study. This study was carried out on population above 10-year age group only. Total 53 smear positives cases of malaria examined out of these 33 were males (62.26 %) and 20 (37.73 %) were females age ranging from 14 years to 70 years. Out of 53 patients 13 (24.52%) patients were died. Amongst these 09 were male and 04 were female. Out of 53 patients 51 (96.22%) cases were falciparum malaria and 2 (03.77 %) were having mixed infection of both species (PF+PV) (Table 1).

Table 1: Distribution of patients according to age, sex, death and incidence of malaria.

Age (10-70)	Sex (n=53)		Death		Incidence of malaria	
Age group	**Male**	**Female**	**Male**	**Female**	**PF**	**PF+PV**
10-20	9	3	1	0	12	0
21-30	10	8	2	2	17	1
31-40	7	4	2	1	11	0
41-50	5	4	2	1	8	1
51-60	1	1	1	0	2	0
>61	1	0	1	0	1	0
Total	33 (62.26%)	20 (37.73%)	9 (16.9%)	4 (7.54%)	51 (96.22%)	2 (3.77%)

$\chi 2$=8.56, p=0.003, considered significant. The/ column association is statistically significant (Male> female, age group 10-30 PF> older age group, PF patients > Mixed, p<0.001, significant as per chi square test)

Out of 53 patients, 23 (43.39%) patients were presented as severe malaria as defined by WHO. Amongst these 14 (60.86%) were male and 09 (39.13%) were female. Amongst severe malaria 11 (47.82%) patients were survived and 12 (52.17%) were died. Amongst survived 8 (72.72%) were male and 3 (25 %) were female. Amongst deaths due to severe malaria 9 (75%) were male and 3 (25%) were female. Out of 53 patients, 05 (09.43%) patients were having others features of severe malaria as defined by WHO (supporting). Amongst these 03 (60 %) were male and 02 (40 %) were female. Amongst these 04 (80 %) patients were survived and 01 (20 %) were died. Amongst survived 02 (50 %) were male and 02 (50 %) were female. Deaths due to this were 01 (20%). Out of 53 patients, 25(47.1%) patients presented as simple (uncomplicated) malaria amongst these 15 (60 %) were male and 10 (40 %) were female amongst this group all has been survived and no death has been reported (Table 2).

Table 2: Prevalence of severe and simple falciparum malaria (WHO).

Type of malaria	Total cases (%)			Survived (%)			Died (%)		
	Male	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total (%)**
Severe	14 (60.8)	9 (39.13)	23(43.39)	8 (72.7)	3 (25)	11(47.82)	9 (75)	3 (25)	12 (52.17)
Simple	15 (60)	10 (40)	25 (47.1)	15 (60)	10 (40)	25 (100)	0	0	0
Controversial*	3 (60)	2 (40)	5 (9.43)	2 (50)	2 (50)	4 (80)	1 (20)	0	1(20)

* Having other features of Severe malaria but not included in guideline of WHO. $\chi 2$ (Chi square) =8.65. DF=2, p=0.001 considered significant. The row and column association is statistically significant. (Severe malaria > controversial P<0.01, simple > controversial, P< 0.01, Severe V/s simple malaria, p>0.58, non-significant) In case severe malaria Male> female P<0.05, significant, died malaria cases significantly higher in severe malaria (P<0.05) as compared to simple malaria.

Out of 53 cases, majority presented as classical symptoms of fever (98.1%), vomiting (66.03%), headache (56.66%), and altered sensorium (33.96%). others presented as diarrhoea (13.20%), convulsion (7.54%), giddiness (5.66%), cough (7.54%), jaundice (9.43%), pain abdomen (13.20%), abnormal gait (1.88%), GI bleeding (7.54%), anorexia (7.54%) and shortness of breath (11.32%). In addition, significantly higher number of patients showed hepatomegaly (30.18 %), anemia (66.03%) and splenomegaly. Rest of patients presented as coma (1.88%), icterus (9.43%), meningial sign (7.54%), mutism (3.77%), cerebellar sign (1.88%), hypotension (3.77%), pulmonary infiltration (26.40%) and retinal hemorrhage (1.88%) (Table 3). As per WHO guideline, poor prognostic biomarkers of falciparum malaria associated with mortality rate has been performed in present study and found that 6 (11.32%) patients were having high (>5%) parasitaemia and all have been died, 03 (5.66%) patients were having schizonts in peripheral

blood film and all have been died, 11(20.75%) patients were having hemoglobin (Hb) <7.1 gm% and amongst these 03 (27.27%) patients were died. Only one patient was having low blood sugar at the time of admission and survived. Two (3.77%) patients had serum creatinine >3.0 mg% and all were died due to renal failure. Four (7.54%) patients had raised SGOT and SGPT and all have been died.

Table 3: Clinical sign and symptoms of *P. falciparum* malaria and their incidence.

Physical signs	Total no of cases (%)	Symptoms	Total no of cases (%)
Splenomegaly	29 (54.71)	Fever	52 (98.11)
Hepatomegaly	16 (30.18)	Vomiting	35 (66.03)
Anemia	35 (66.03)	Headache	30 (56.66)
Coma	1 (1.88)	Sensorium	18 (33.96)
Icterus	5 (9.43)	Diarrhoea	7 (13.20)
Meningial sign	4 (7.54)	Convulsion	4 (7.54)
Mutism	2 (3.77)	Giddiness	3 (5.66)
Cerebellar	1 (1.88)	Cough	4 (7.54)
Hypotension	2 (3.77)	Jaundice	5 (9.43)
Pulmonary infiltration	14 (26.40)	Pain abdomen	7 (13.20)
Retinal hemorrhage	1 (1.88)	Abnormal gait	1 (1.88)
*Statistical analysis done by SPSS windows version in percentages or frequency		GI bleeding	4 (7.54)
		Anorexia	4 (7.54)
		Shortness of breath	6 (11.32)

Conclusively out of 53 patients 29 (54.71%) patients were having laboratory indices of poor prognosis and amongst them 19 (65.51%) patients were died. Thus, our findings confirm that patients who had P. falciparum malaria with laboratory indices of poor prognosis had high incidence of mortality (Table 4).

Table 4: Poor prognostic biomarkers and major predictors with mortality in *P. falciparum* malaria patients.

Poor prognostic biomarkers with mortality			Major predictors with mortality		
Biomarkers	**Patients (%)**	**Mortality (%)**	**Predictor**	**Patients (%)**	**Mortality (%)**
High parasitaemia	6 (11.32)	6 (100)	ARDS	9 (16.98)	7 (77.7)
Schizont in PBF	3 (5.66)	3 (100)	Severe anemia	7 (13.20)	3 (42.8)
TLC > 12,000	2 (3.77)	1 (50)	Jaundice	5 (9.43)	4 (80)
HB<7.1 gm%	11 (20.75)	3 (27.2)	Imp. Consciousness	18 (33.36)	8 (44.44)
Blood sugar <40 mg %	1 (1.8)	0 (0)	*2 cells (12.6%) have expected count less than 5. The minimum expected count is 3.45. (the p value <0.001). The row and column variable are significantly associated. As per χ^2=26.32, DF=6, p<0.01, poor prognostic biomarkers and major predictors were significantly sturdily associated with mortality rate (p<0.0001)		
Serum creatinine >3 mg%	2 (3.77)	2 (100)			
Increase SGOT and SGPT	4 (7.54)	4 (100)			
Total	29 (54.7)	19 (65.5)			

Clinical assessment

All the patients were assessed according to the WHO criteria for severe and complicated malaria, which consist of 10 defining clinical or laboratory criteria, supported by 5 additional non-defining criteria (Table 5). Out of 53 patients, 09 (16.98%) patients presented as acute respiratory distress syndrome (ARDS), out of which 07 (77.77%) patients were died. 07 (13.20%) patients were presented as severe anemia, out of which 03 (42.84%) patients were died.

05 (09.43%) patients presented as Jaundice, out of which 04 (80%) patients were died. 18 (33.36%) patients were presented as an impaired consciousness, out of which 08 (44.44%) patients were died (Table 4).

In our study group total 53 patients were studied. Amongst these 13 (24.52%) patients died. Major contributors to mortality was impaired level of consciousness, anemia, ARDS and jaundice at the time of presentation. These were used to construct simple prognostic indices in falciparum malaria. Malaria with impaired level of consciousness was present in 18 (33.96%) patients and out of these 8 (44.4%) patients were died. Malaria with ARDS was present in 09 patients, malaria with anemia 07 patients and malaria with jaundice in 05 patients. One patient was having overlap features of anemia, jaundice, impaired level of consciousness, ARDS was died. One patient was having overlap features of anemia jaundice, and impaired level of consciousness, was died. Two patients were having overlap features of ARDS jaundice, and impaired level of consciousness, were died. One patient was having overlap features of anemia with jaundice, and impaired level of consciousness, was survived (Table 5).

Table 5: Frequency and morality of severity (condition of severe Malaria) in falciparum malaria (as per WHO guideline).

Criteria /guideline	Total no of patients and frequency (%)	Mortality rate (%)
Coma	1 (1.8)	1 (100)
Severe anemia	7 (13.20)	3 (42.85)
Renal failure	2 (3.77)	2 (100)
ARDS	9 (16.98)	7 (77.7)
Hypoglycemia	1 (1.8)	0 (0)
Circulatory collapse	1 (1.8)	0 (0)
Spontaneous bleeding	4 (7.54)	2 (50)
Repeated convulsion	1 (1.8)	1 (100)
Haemoglobinuria	1 (1.8)	1 (100)
Five supporting criteria		
Impaired consciousness	18 (33.96)	8 (44.4)
Prostration	26 (49.0)	2 (7.66)
Hyperparasitaemia	6 (11.32)	3 (50)
Jaundice	5 (9.43)	4 (80)
Hyperpyrexia	3 (5.66)	0 (0)

As per $\chi 2=12.56$., DF=8, $p<0.01$, (2 cells (25.36%) have expected count less than 5. The minimum expected count id 2.86 (P value 0.002 considered significant. The row / column variable is significantly associated), Feathers of severe malaria like Anemia ($P<0.05$), renal failure ($p<0.05$), ARDS ($P<0.05$), Impaired consciousness ($p<0.05$) and hyperparasitamia ($P<0.05$) were significantly and strongly associated with mortality rate in falciparum malaria.

DISCUSSION

Research in malaria today has assumed a degree of urgency perhaps not equaled at any time before. Falciparum malaria can affect all age groups including neonates. In our study 53 smear and rapid diagnostic test positive cases were examined, amongst these male's patients (62.62%) were higher as compared to female's patients (37.73%). Falciparum malaria was significantly higher in lower age groups (10-30 years) than higher age groups (>31 years). Out of 53 patients 13 (24.52%) patients died. Falciparum malaria as such is a disease of protean clinical manifestations. In our study majority of cases were presented as classical symptoms of fever (98.1%), vomiting (66.03%), headache (56.66%), and altered sensorium (33.96%). Others presented as diarrhoea (13.20%), convulsion (7.54%), giddiness (5.66%), cough (7.54%), jaundice (9.43%), pain abdomen (13.20%), abnormal gait (1.88%), GI bleeding (7.54%), anorexia (7.54%) and shortness of breath (11.32%).

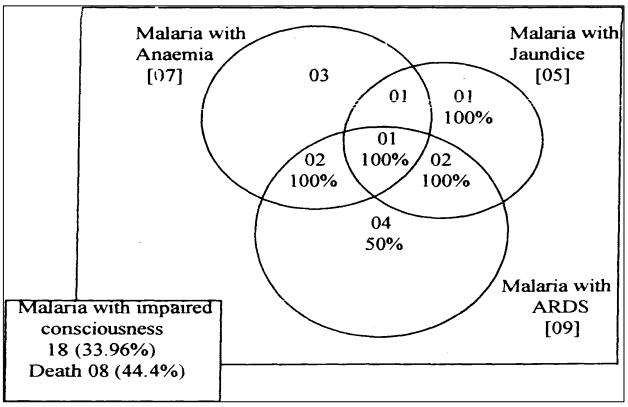

Figure 1: Prevalence overlap and mortality for major clinical sub group of sever malaria. Total numbers are given in parenthesis and mortality is given as percentage.

1.89% cases were febrile, which is quite lower than observed in another study.[22] The absence of fever can be accounted by either presence of milder form of infection or occurrence of chronic infection. Cerebral involvement in falciparum malaria is one of the serious complications and it was observed in about 33.96% cases and mortality rate was 44.4% in our study which is accordance with earlier study.[23]

The most prominent feature of cerebral malaria is dense parasite sequestration within cerebral blood vessels, cyto-adherence of parasitized red blood cells to endothelial cells to non-infected erythrocytes may contribute to pathogenesis of cerebral malaria by compromising the cerebral circulation.[24,25]

In our study 1.88% cases presented with cerebellar features, 1.88% cases as coma 3.77% cases presented as mutism and meningeal sign found in 7.54% cases. The pathogenesis of cerebellar malaria is same as that of cerebral malaria. Convulsions were presented in 7.54% cases. The sequestration may be lead to tissue anoxia, hypoglycemia, which is responsible for convulsion. Gastrointestinal symptoms presented as pain abdomen 13.20%, diarrhea 13.20%, anorexia 7.54% and gastrointestinal bleeding in 7.54% cases in our study. Gastrointestinal symptoms including bleeding occurs in

malaria as a result of invasion of gastrointestinal vasculature and sloughing of gut mucosa and catarrh.[26]

In present study, Jaundice was seen in 9.43% cases and this is mostly due to malarial hepatitis and cholestasis and responsible for mortality in malaria. In our study out of 05 patients of jaundice 04 (80%) patients were died which was consistent with most recent previous study.[6]

Pulmonary infiltrations were observed in 26.40 % cases. Out of these 19 cases (16.98%) were presented as ARDS and amongst these 07 cases (77.77%) were died. Thus, ARDS is responsible for increase mortality in falciparum malaria. These findings are similar to an observational study done by Bernard et al in United States of America.[27]

Involvement of kidney is well known in falciparum malaria as acute renal failure, black water fever, glomerulonephritis and nephrotic syndrome. In our study, acute renal failure was observed in 3.77% cases and 1.88% cases were presented as haemoglobinuria.

In addition, renal involvement contributes to 100% mortality rate in falciparum malaria in spite of dialysis and exchange transfusion. The outcomes of present study are agreed with a case control study performed by Khuraiya et al in central (M. P) India.[28] This is because of delay in referral services and high level of parasitaemia in blood.

In our study 54.71% cases had hepatomegaly and 30.18% had splenomegaly which is accordance with recent interventional observation study done in India and it observed that 50.92% patients had hepatomegaly and 31.69% had splenomegaly. This is caused by vascular congestion and reticuloendothelial proliferations.[28]

Anemia is frequent presenting features of malaria and it was observed in 66.03% cases which are quite higher than observed in another study.[22] However, similar result was observed in two Indian studies conducted by Hussain et al who found higher prevalence of anemia in (60.52%) falciparum malaria patients and another study from central India (M.P) reported that 57% patients had normocytic normochromic anemia.[28,29]

The pathogenesis of anemia is complex and multifactorial. The mechanism is destruction of parasitized red blood cells, malaria antigen attachment to erythrocytes followed by their immunological lysis and destruction of newly synthesized erythrocytes by TNF.[30,31]

Out of these patients of anemia with malaria 03 (42.03%) cases were died. Thus, anemia is responsible for increase mortality in malaria. Retinal hemorrhages seen in 1.88% cases were probably due to thrombocytopenia. Comparable observation was found in North western Indian study performed by Kocher et al and reported retinal hemorrhage in 2.5% patients and thrombocytopenia was observed in 26% of patients.[6] Hypotension were seen in 3.77% cases. Similar observation was found in the population based Indian study.[32] Hypotension is because of dehydration and hyponatremia.[33]

Limitation of our study is that systemic inflammatory marker TNF-α and plasma bicarbonate ions (Hco^{3-}) which are laboratory indices of poor prognosis and feature of severity and prognosis of falciparum malaria, respectively were not measured in this study. In addition, this is an observational study and further molecular research or state of anti-malarial drugs sensitivity and clinical studies with large sample size are required to investigate reason of materialization of severe malaria and mortality rate in falciparum malaria.

CONCLUSION

The present study showed a high prevalence of severe malaria (43.39%) and mortality rate (65.51%) in *P. falciparum*. Majority of cases were presented as classical symptoms of fever, vomiting, headache, and altered sensorium. In addition, patients having severe and complicated malaria feature overlapping with anemia (13.32%), ARDS (16.98%), Jaundice (9.43%) and impaired consciousness (32.96%).

Therefore, these four features were responsible for high incidence of mortality in malaria (24.53%). Laboratory indices of poor prognosis in falciparum malaria were significantly associated with mortality rate.

We found that 11.32% patients were having high (>5%) parasitaemia, 5.66% patients were having schizonts in peripheral blood film, 20.75% patients were having hemoglobin (Hb) <7.1 gm%, 3.77% patients had serum creatinine >3.0 mg%. 7.54% patients had raised SGOT and SGPT and all have been died. Overwhelmingly 29 (54.71%) patients were having laboratory indices of poor prognosis and amongst them 19 (65.51%) patients were died. Consequently, our finding confirms that patients who had *P. falciparum* malaria with laboratory indices of poor prognosis had high incidence of mortality.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Khatib Y, Patel R, Sequeria K, Agrawal G, Chikhale N. Hematological and biochemical alterations in malaria and their correlation with Parasitic Index. IOSR J Pharm. 2015;5(9):53-6.
2. Verma RK, Giri R, Singh N, Verma S, Shrivastav V. A study on clinical presentation and outcome of malaria from an underreported, *p. vivax* predominant region of north India. Sch. J. App. Med. Sci. 2016;4(1):233-43.

3. Park JE, Park K: Text Book of preventive and social medicine: Malaria, 23 editions. Jabalpur (MP) India: Banarsidas Bhanot Publishers. 2015;15:188-202.
4. WHO. Eight report on the world health situation-Implementation of the global strategy for health for all by the year 2000, Second evaluation volume for South East Asia Regio,2000. Available at http://apps.who.int/iris/handle/10665/37640.
5. World Health Organization. Universal access to malaria diagnostic testing: an operational manual, WHO, Geneva Switzerland, 2011. Available at http://www.who.int/malaria/publications/atoz/9789241502092/en/.
6. 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.
7. Bhalli MA. P. falciparum malaria-A review of 120 cases. J Coll Physicians Sur Pak. 2001;11:300-3.
8. Mohapatra MK. The natural history of complicated falciparum malaria-A prospective study. J Ass Physicians India. 2006;54:848-53.
9. Field JW, Niven JC. A note on prognosis in relation to parasite count in acute sub tertian malaria. Trans R So Trop Med Hyg. 1937;30:569-74.
10. Mangal P, Mittal S, Kachhawa K, Agrawal D, Rath B. Analysis of the clinical profile in patients with plasmodium falciparum malaria and its association with parasite density. J Glob infects Dis. 2017;9(7):60-5.
11. Das LK, Padhi B, Sahu SS. Prediction of outcome of severe falciparum malaria in Koraput, Odisha, India: A hospital-based study. Tropical Parasitol 2014;4(2):105-10.
12. Bojang KA, Van Hensbroek MB, Palmer A, Banya WA, Jaffar S, Greenwood BM. Predictors of mortality in Gambian children with severe malaria anaemia. Ann Trop Paedia. 1997;17:355-9.
13. Marsh K, Forster D, Waruiru C, Mwangi I, Winstanley M, Marsh V, et al. Indicators of life-threatening malaria in African children. N Eng J Med. 1995;332:1399-404.
14. Schellenberg D, Menendez C, Kahigwa E, Font F, Galindo C, and Acosta C, et al. African children with malaria in an area of intense Plasmodium falciparum transmission: Features on admission to the hospital and risk factors for death. Am J Trop Med Hyg. 1999;61:431-8.
15. World Health Organization. Severe and complicated malaria. Trans R Soc Trop Med Hyg. 1990;84(suppl 2):S1-S65.
16. World Health Organization. Severe falciparum malaria. Trans R Soc Trop Med Hyg. 2000; 94(suppl 1):S1-S90.
17. Adams ARD, Maegraith BG. Clinical Tropical Diseases: Malaria. 9th edition. UK: Wiley Blackwell. 1989;20:427-42.
18. Facer C, Cook G. Parasites in blood and faeces. In: Swash M, Glynn M, Drake WM (editors). Hutchison's Clinical Methods, 23ed., Bristol, UK. Saunders. 1995;36:427-42.
19. Warhurst DC, Williams JE. Laboratory Diagnosis of Malaria. J ClinPathol. 1996;49:533-8.
20. Hansheid T. Diagnosis of malaria: A review of alternatives to conventional microscopy. Clin Lab Haematol. 1999;21:235-45.
21. Wilkinson RJ, Brown JL, Pasvol G, Chiodini PL, Davidson RN. Severe falciparum malaria: predicting the effect of exchange transfusion. Q J Med. 1994;87:553-7.
22. Chandar V, Mehta SR, Sharma PD, Sarkar PK, Sharma BR. Falciparum malaria. Ind J pediatrics. 1989;56(3):365-9.
23. Angyo IA, Pam SD, Szlachetka R. Clinical pattern and outcome in children with acute severe falciparum malaria at Jos University Teaching Hospital, Nigeria. East Afr Med J. 1996;73:823-6.
24. Udeinya IJ, Schmidt JA, Aikawa M, Miller LH, Green I. Falciparum malaria-infected erythrocytes specifically bind to cultured human endothelial cells. Science. 1987;212:555-57.
25. David PH, Handunnetti HM, Leech JH, Gamage P, Mendis KN. Rosetting: a new cytoadherence property of malaria-infected erythrocytes. Am J Trop Medic Hyg. 1988;38(2):289-297.
26. Vollar L. Immunopothology of malaria, Bull WHO. 1974;50:177-186.
27. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. Report of the American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. The Consensus Committee. Intensive Care Med. 1994;20:225-32.
28. Khuraiya P, Sharma SS, Thakur AS, Pandey VP, Verma S. The study of clinical, biochemical and hematological profile in malaria patients. Int J Adv Med. 2016;3:209-17.
29. Hussian MM, Sohali M, Abhishek K, Raziuddin M. Investigation on Plasmodium vivax infection influencing the host factors in tribal dominant and malaria endemic population of Jharkhand. Saudi J Biol Sci. 2013;20(2):195-203.
30. Jeje OM, Kelton JG and, Blajehman MA. Quantitation of red cell membrane associated immunoglobulin in children with *Plasmodium falciparum* parasitaemia. Brit J Hematol. 1983;54:567-572.
31. Weatherall DA, Abdalla S. The anemia of Plasmodium falciparum malaria. Brit Medic Bulletin. 1982;38(2):147-151
32. Galande CJ, Desai RR, Aundhakar SC, Patange AP, Goel UK. Study of clinical profile of malaria in tertiary referral centre in western Maharashtra. Inter J Heal Sci Res (IJHSR). 2014;4(3):51-8.
33. Brooks MH, John P, Mathy, Peter JB, William DT, Thomas WS et al. The pathophysiology of acute falciparum malaria. Correlation of clinical and biochemical abnormalities, Am. J. Med. 1967;43:735-43.

Cite this article as: Choudhary H, Choudhary PR. Study of clinical presentation of falciparum malaria and correlation with laboratory indices of poor prognosis. Int J Adv Med 2017;4:1591-8.