ORIGINAL ARTICLE

Biochemical Spectrum of *Plasmodium falciparum* Malaria

Sanjay Deshwali[1], Akanksha Dubey[2]

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Abstract

Background: Malaria continues to pose significant health challenges globally, with *Plasmodium falciparum* being the most virulent species contributing to severe complications. This study aims to evaluate the biochemical manifestations of *P. falciparum* malaria in a tertiary care hospital setting.

Materials and methods: A hospital-based cross-sectional study was conducted to assess the biochemical profile of patients diagnosed with *P. falciparum* malaria. Patients above 12 years of age presenting with fever and confirmed positive for *P. falciparum* on peripheral smear were included. Patients with comorbid conditions or other identifiable causes of fever were excluded from the study.

Results: Among 962 patients admitted for febrile illness, 100 met the inclusion criteria. The most common clinical feature observed was chills and rigors (82%), followed by headache (42%) and vomiting (36%). Complications included cerebral malaria in 38% of patients, severe anemia (10%), oliguria (26%), acute respiratory distress syndrome (1%), hypoglycemia (8%), shock (12%), bleeding manifestations (4%), generalized tonic–clonic seizure (6%), hemoglobinuria (11%), hyperparasitemia (80%), hyperpyrexia (42%), and jaundice (24%).

Conclusion: *Plasmodium falciparum* malaria presents with a diverse biochemical and clinical spectrum, often leading to multiorgan dysfunction. Early recognition and prompt management are essential, and malaria should be considered in patients presenting with febrile illness and systemic complications. This study underscores the importance of vigilant diagnostic approaches in endemic regions.

Keywords: Biochemical spectrum, Cerebral malaria, Malaria, *Plasmodium falciparum*, Tertiary care hospital.

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Introduction

Malaria is a disease of global importance that results in 500 million cases and 1.5–2.7 million deaths yearly. Approximately, 2.48 million are reported from South East Asia, of which 75% are reported from India. It is responsible for major morbidity and mortality. It presents with various presentations. Drug resistance and demographic development further increases malaria morbidity and mortality. The present study was done to see biochemical spectrum of falciparum malaria (Table 1). A major cause of concern for the world and India. The disease's significant morbidity and mortality are caused by its varied presentations, medication resistance, and demographic shifts. *P. falciparum* malaria has been linked to serious consequences, including death. The clinical and epidemiological characteristics of malaria has changed significantly in the past several years when compared to earlier times. Despite attempts to prevent and control malaria, the disease remains a substantial concern in the Asia-Pacific area. Malaria caused by *P. falciparum* is a critical public health concern with severe effects. *P. falciparum* is the most dangerous Thus the study's findings will provide significant insights, improving our understanding of healthcare dynamics and allowing for more targeted and successful interventions for this specific group.[1–5]

Materials and Methods

All patients who presented with history of fever and were above 12 years of age, who were positive for *Plasmodium falciparum* on peripheral smear and did not have any comorbid conditions or localizing factors for fever were included in this study. A detailed history and examination were done on patients in the study groups, and relevant details were recorded on a predesigned proforma.

[1]People's College of Medical Sciences and Research Centre, Bhopal, Madhya Pradesh, India

[2]Department of Biochemistry, Gujarat Medical Education & Research Society Medical College, Vadnagar, Gujarat, India

Corresponding Author: Akanksha Dubey, Department of Biochemistry, Gujarat Medical Education & Research Society Medical College, Vadnagar, Gujarat, India, Phone: +91 8871102287, e-mail: akanksha.dby@gmail.com

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All patients were investigated for complete blood count, fasting blood sugar, blood urea, serum creatinine, serum electrolytes, urine routine and microscopy test, serum bilirubin, liver enzymes, and prothrombin time (PT). Cerebrospinal fluid (CSF) examination, computed tomography scan, ultrasonography (USG) of abdomen, and chest X-ray were done where and when required.[6]

Results

A total of 100 patients meeting the inclusion criteria were thoroughly evaluated and documented using a specially designed proforma. Peripheral blood smears were analyzed, confirming the diagnosis. During the study period, 962 cases of pyrexial illnesses were admitted, of which 413 patients (43%) were clinically diagnosed and treated for malaria. Peripheral smear positivity was observed in 180 patients (18.89%). Among the positive cases, *P. falciparum* accounted for 55.55%, *P. vivax* for 32.15%, and mixed

Table 1: Laboratory findings

S. No.	*Lab findings*	*Male*	*Female*	*No. of cases*	*%*
1.	Blood sugar <40 mg%	3	5	8	8
2.	Hemoglobin%				
	≤5.0 gm%	4	6	10	10
	5.1–10.0 gm%	30	26	56	56
	≥10.1 gm%	26	8	34	34
3.	Total leukocyte count (cells/mm^3)				
	≤4,000–11,000	55	33	88	88
	4,000	2	2	4	4
	≥11,000	3	5	8	8
4.	Differential leukocyte count				
	Polymorphocytosis (>74%)	18	5	23	23
	Lymphocytosis (>45%)	5	1	6	6
5.	Renal function test				
	Blood urea (mg/dL)				
	<40	48	26	74	74
	40–60	4	4	8	8
	60–100	8	8	13	13
	>100	0	2	2	2
	Serum creatinine (mg/dL)				
	<1.5	40	30	70	70
	1.5–3	16	4	20	20
	>3	4	6	10	10
	Serum sodium (mEq/L)				
	>145	1	2	3	3
	<120	6	4	10	10
	Serum potassium (mEq/L)				
	>6	6	2	8	8
	<3	1	1	2	2
6.	Liver function test (mg/dL)				
	Serum bilirubin (T > 1.0, D > 0.3)				
	<1	40	30	70	70
	1–5	12	6	18	18
	>5	8	4	12	12
	Increased SGOT (>35 IU/L)	20	6	26	26
	Increased PT				
	(International normalized ratio derangement)				
	<2	40	30	70	70
	2–4	8	8	16	16
	4–6	2	2	4	4
	>6	0	0	0	0
7.	Urine routine and microscopy				
	Hemoglobinuria	8	3	11	11
	Albumin (+)	28	8	36	36
	RBCs (+)	0	0	0	0
8.	Platelet count				
	(<1.5 lakhs/mm^3)	26	8	34	34

(Contd...)

Table 1: *(Contd...)*

S. No.	*Lab findings*	*Male*	*Female*	*No. of cases*	*%*
9.	Chest X-ray				
	Pneumonitic patch	0	0	0	0
	B/L pulmonary edema	0	1	1	1
10.	USG of abdomen				
	Hepatomegaly	20	8	28	28
	Splenomegaly	6	3	9	9
	Hepatosplenomegaly	5	4	9	9
11.	CT head ($n = 12$)				
	Infract	1	0	1	1
	Cerebral edema	2	1	3	3
	Within normal limits	5	3	8	8
12.	CSF examination ($n = 28$)				
	Opening pressure raised	2	0	2	2
	Decreased glucose (<40 mg/dL)	0	0	0	0
	Increased proteins (>50 mg/dL)	2	0	2	2
	Increased cells (>5/mL)	0	0	0	0

Table 2: Relative frequencies of severity (as per World Health Organization guidelines)

S. No.	*Complications*	*No. of cases*	*%*
1.	Cerebral malaria (coma/impaired cause) not attributable to any other cause	38	38
2.	Severe anemia (hemoglobin <5 gm/dL)	10	3
3.	Oliguria or serum creatinine >3 mg/dL	26	26
4.	ARDS	1	1
5.	Hypoglycemia (random blood sugar <40 mg/dL)	8	8
6.	Shock (systolic blood pressure <80 mm Hg)	12	12
7.	Bleeding manifestation	4	4
8.	Generalized tonic–clonic seizure (>2 in 24 hours)	6	6
9	Hemoglobinuria	11	11
10.	Hyperparasitemia (3+ or more)	80	80
11.	Hyperpyrexia (rectal temperature <104° F)	42	42
12.	Extreme weakness without neurological cause	4	4
13.	Jaundice (total bilirubin >3 mg/dL)	24	24

infections for 12.35%. Male patients constituted 60%, while 40% were female. The highest incidence (52%) was recorded in the 21–40 year age-group. Seasonal variation revealed peak incidence (76%) during July to October.

Fever was the predominant symptom, present in 100% of cases, followed by chills and rigors (82%), headache (42%), vomiting (36%), altered sensorium (40%), jaundice (22%), decreased urine output (18%), seizures (16%), and bleeding manifestations (4%). Complications were correlated with fever duration and intensity. Notably, 90.47% (76 out of 84) of patients with complications had fever lasting more than 3 days. High-grade fever was associated with systemic complications in 74% of cases. Intermittent fever was the most common pattern (62%), followed by irregular fever (36%) and continuous fever (2%).

Pallor was observed in 64% of patients, and icterus in 30%. Respiratory system examination revealed hyperventilation in 20% of patients, with acute respiratory distress syndrome (ARDS)-like features in 1%. Cardiovascular assessment showed sinus tachycardia in 92%. Hepatomegaly was noted in 24%, splenomegaly in 6%, and hepatosplenomegaly in 6%. Decreased urine output was present in 18%, with 14% experiencing oliguria and 11% reporting hemoglobinuria. Neurological evaluation revealed altered sensorium in 40% of patients, with 16% stuporous, 12% drowsy, and 12% comatose. Hemiparesis was identified in two patients (Table 2).

Hypertonia was noted in 6% of patients, hypotonia in 3%, brisk deep tendon reflexes in 12%, and sluggish or absent reflexes in 6%. Plantar response was extensor in 6%, not elicitable in 7%, and withdrawal in 3%. Cerebellar signs were positive in 2% of cases.

Among 38 patients with cerebral malaria, retinal hemorrhage was observed in 8%, papilledema in 4%, disc pallor in 20%, and hyperemia in 3%.

Hypoglycemia was noted in 8% of patients. Hemoglobin levels were below 5 g/dL in 10%, and between 5 and 10 g/dL in 56%. Total leukocyte counts exceeded 11,000/mm^3 in 4%, while 3% had counts below 4,000/mm^3. Serum creatinine was elevated in 30% of patients, and blood urea in 28%. The highest recorded urea level was 182 mg/dL, and maximum creatinine was 9.5 mg/dL. Serum bilirubin was elevated in 30% of cases, while serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic-pyruvic transaminase (SGPT) levels were raised in 25% of patients each. Prolonged PT was detected in 30%. Urinalysis revealed albumin in 36% and hemoglobinuria in 11%. Platelet counts below 1.5 lakhs were found in 34% of patients.[7–16]

Chest X-ray indicated ARDS-like features in one patient. Abdominal USG demonstrated splenomegaly in 9%, hepatomegaly in 28%, and hepatosplenomegaly in 9%. Acute renal parenchymal disease was evident in 12 patients. Computed tomography scans of the head (performed in 12 patients) revealed cerebral edema in one patient and acute infarction in the left frontoparietal region in another. The CSF analysis (conducted in 28 patients) showed raised opening pressure in one patient, with normal glucose levels across the cohort. Elevated protein levels (50–60 mg/dL) were identified in two patients. Cell counts remained within normal limits.[17]

The observed mortality rate was 16% (12 patients), predominantly due to multiorgan involvement. Neurological complications were present in 100% of fatal cases, alongside renal (66%), hepatic (100%), hematological (100%), and shock (50%) complications. Artemisinin derivatives were administered to 36% of patients, quinine to 64%, and doxycycline to 22.67%, either alone or in combination.[18–21]

This study highlights the clinical spectrum and complications associated with *P. falciparum* malaria, emphasizing the importance of early diagnosis and prompt management to reduce mortality and morbidity.[14]

Discussion

Falciparum malaria is a significant cause of life-threatening complications, necessitating heightened clinical vigilance in tropical regions. Early detection of malarial symptoms and signs is crucial to prevent progression to severe outcomes. Over a 12-month period, 7,952 patients were admitted to the medical wards of Hamidia Hospital, with 962 presenting pyrexial illnesses.[21] After excluding nonmalarial febrile conditions, 413 cases were clinically diagnosed and treated as malaria, and malarial parasites were identified in 180 patients. Among these, 100 patients (55.55%) were infected with *P. falciparum*, 57 (32.15%) with *P. vivax*, and 23 (12.35%) exhibited mixed infections.

Table 2 shows that most common complication apart from hyperparasitemia in falciparum malaria is hyperpyrexia, followed by cerebral malaria (most of the patients in the study had more than one complication).

A notable increase in *P. falciparum* cases was observed, rising from 21% in 1982 to 41% in 1992. By 2005, the incidence reached 52.3% (WHO, 2002; Park, 2005). Data from the Malaria Research Center field station in Jabalpur corroborated this trend, with *P. falciparum* infections increasing from 27% in 1989 to 60% by 2000 in Mandla district villages.

Multiple studies (Senanayake and de Silva and Nguyen et al.) have reported higher *P. falciparum* prevalence compared with *P. vivax*.[18] This shift is attributed to increasing chloroquine resistance in *P. falciparum* strains, while *P. vivax* remains susceptible to treatment. Proximity to Southeast Asian regions, such as Thailand, Cambodia, Myanmar, and Laos, where *P. falciparum* demonstrates <10% sensitivity to sulfapyrimethamine, may contribute to this trend. The preponderance of severe falciparum cases at Hamidia Hospital is likely influenced by its status as a tertiary referral center, resulting in higher admissions for complicated cases, whereas less-severe *P. vivax* infections are managed at peripheral health centers and district hospitals. Malaria affected all age-groups, but this study included patients older than 12 years, with the highest incidence (52%) occurring in individuals aged 21–40 years. Mean age ± 2 standard deviation was 37.12 ± 14.42 years for males and 33.26 ± 10.24 years for females. Incidence declined with age, reflecting delayed acquisition of immunity (premunition) and increased outdoor exposure in younger populations (Bradley et al., 1996). Similar findings were reported by Garg, Banerjee et al., and Parteti et al.[8]

Male predominance (60%) was observed, potentially due to greater outdoor exposure, protective clothing among females, or genetic factors linked to the X chromosome. Comparable gender disparities were noted by Dhamija, Garg, and Manuhan et al.[8] Seasonal variation was evident, with 56% of cases occurring during the postmonsoon period (July–October), correlating with optimal parasite development and mosquito breeding.[15] Lower incidence during cooler months (January–February) reflects suboptimal conditions for parasite transmission. Fever was the most prevalent symptom, affecting 100% of patients. This aligns with reports by Anjali et al. (1985) and Murali et al. (2000). Intermittent fever predominated (62%), consistent with Singh et al. and Jao et al. Prolonged fever (>7 days) was associated with systemic complications in 91.7% of cases ($p < 0.05$). High-grade fever (>104°F) occurred in 42%, with systemic involvement in 31 cases.[16]

Additional symptoms included chills and rigors (82%), headache (62%), vomiting (36%), and altered sensorium (38%). The latter met WHO criteria for cerebral malaria, aligning with prior findings (Sowunmi, 0.01–16%; Sanchetae and Varma, 0.8–1.5%).[15] Convulsions occurred in 12%, with six patients experiencing more than two seizures within 24 hours. Additional manifestations included jaundice (22%), reduced urine output (18%), anemia (64%), and hepatosplenomegaly (6%).[16]

Laboratory findings revealed hemoglobin <10 gm/dL in 75 patients, with normocytic normochromic anemia in 32 cases. Serum bilirubin >1.0 mg/dL was observed in 30%, while elevated SGOT and SGPT levels were present in 25% of patients. Elevated blood urea and serum creatinine were noted in 26% and 30%, respectively, correlating with acute renal failure. Neurological assessments identified altered consciousness in 40% of patients, with coma in 12%. Retinal hemorrhages (8%) and papilledema (4%) were observed in cerebral malaria cases. The CSF analysis in 28 patients revealed normal glucose and cell counts, with elevated proteins in two cases. Computed tomography imaging identified cerebral edema in three patients and infarcts in one.[15]

The evolving clinical spectrum of severe falciparum malaria, with increasing incidence of jaundice and renal failure, underscores the importance of early diagnosis and appropriate management to mitigate mortality and morbidity.[9,17–22]

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