International Journal of Research in Medical Sciences
Mehta B et al. Int J Res Med Sci. 2026 Aug;14(8):3352-3357
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20262621

Original Research Article

Serum lactate levels as a marker of clinical severity in malaria: a prospective observational study

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Received: 15 May 2026
Revised: 14 June 2026
Accepted: 02 July 2026

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ABSTRACT

Background: Malaria remains a major cause of morbidity and mortality in tropical countries. Severe malaria is associated with microcirculatory dysfunction, tissue hypoxia, and metabolic derangements. Serum lactate may serve as an early marker of disease severity and prognosis. Objectives were to evaluate serum lactate levels in patients with malaria and assess their association with disease severity and clinical outcomes.
Methods: This prospective observational study included 100 adult patients with laboratory-confirmed malaria admitted to a tertiary care hospital. Clinical evaluation and laboratory investigations, including serum lactate estimation at admission, were performed. Disease severity was classified according to WHO criteria. Clinical outcomes were categorized as favorable or adverse.
Results: Of the 100 patients, 48% had *Plasmodium vivax* infection, 42% had *Plasmodium falciparum* infection, and 10% had mixed infection. Patients with severe malaria had significantly higher serum lactate levels than those with uncomplicated malaria (4.5±1.2 vs. 1.6±0.4 mmol/l; p<0.001). Elevated lactate levels were associated with hypotension, severe anemia, metabolic acidosis, renal dysfunction, altered sensorium, hepatic dysfunction, thrombocytopenia, and hypoglycemia. Adverse outcomes occurred in 45% of patients, including ICU admission (22%), prolonged hospital stay (18%), and mortality (8%). Serum lactate levels were significantly higher in patients with adverse outcomes than in those with favorable outcomes (4.5±1.2 vs. 1.6±0.4 mmol/L; p<0.001).
Conclusions: Serum lactate is significantly associated with disease severity and adverse clinical outcomes in malaria. Early lactate estimation may help identify high-risk patients and guide timely management.

Keywords: Malaria, Serum lactate, Severe malaria, Hyperlactatemia, Prognosis

INTRODUCTION

Malaria remains a major public health problem in tropical and subtropical regions, contributing significantly to morbidity and mortality worldwide. Despite substantial advances in diagnosis and treatment, severe malaria continues to pose a major clinical challenge, particularly in endemic countries such as India. Both *Plasmodium falciparum* and *Plasmodium vivax* infections can lead to severe disease manifestations, including multi-organ dysfunction and death.[1-3]

Severe malaria is characterized by complex pathophysiological processes, including microvascular obstruction, impaired tissue perfusion, metabolic acidosis, and organ failure. Sequestration of parasitized erythrocytes within the microcirculation, endothelial dysfunction, reduced red blood cell deformability, and dysregulated inflammatory responses contribute to impaired oxygen delivery at the tissue level.[4,7] These mechanisms result in tissue hypoxia and a shift toward anaerobic metabolism, leading to increased production and accumulation of lactate.

Serum lactate is a well-established biomarker of tissue hypoxia and impaired perfusion in critically ill patients. In conditions such as sepsis and shock, elevated lactate levels are associated with disease severity and increased mortality.[11,12] In malaria, hyperlactatemia has been shown to correlate strongly with metabolic acidosis, organ dysfunction, and adverse outcomes, particularly in severe *P. falciparum* infection.[4-6] Studies in both adults and children have demonstrated that elevated serum lactate levels are predictive of poor prognosis and mortality.[4-6,9]

Previous studies have also shown that hyperlactatemia in malaria is associated with key clinical severity parameters, including hypotension, severe anemia, hypoglycemia, renal dysfunction, and altered sensorium.[5,6,8,10] In addition to increased lactate production due to tissue hypoxia, impaired hepatic clearance and heightened inflammatory responses further contribute to elevated lactate levels in severe disease.[7,10]

Early identification of patients at risk of severe disease and adverse outcomes is critical for timely intervention and improved survival. The World Health Organization (WHO) recommends prompt recognition and management of severe malaria to reduce mortality.[1,2] Serum lactate estimation is a simple, rapid, and widely available investigation that can be performed at the time of hospital admission. Its potential role in early risk stratification and prognostication in malaria warrants further evaluation, particularly in resource-limited settings.

Although several studies have evaluated the prognostic significance of serum lactate in malaria, data from the Indian subcontinent remain limited, especially studies including both *P. falciparum* and *P. vivax* infections. Therefore, the present study was undertaken to evaluate serum lactate levels in patients with malaria and to assess their association with clinical severity and outcomes.

METHODS

Study design and setting

This prospective observational study was conducted in the Department of General Medicine at a tertiary care hospital in North Delhi, India, from June 2022 to June 2023. The study was undertaken as part of the author's postgraduate dissertation in General Medicine.

Study population

A total of 100 adult patients with laboratory-confirmed malaria admitted during the study period were consecutively enrolled. All enrolled patients were included in the final analysis.

Inclusion criteria

Patients with age ≥18 years, laboratory confirmation of malaria by peripheral blood smear and/or rapid diagnostic test and provision of written informed consent were included in study.

Exclusion criteria

Coexisting conditions known to independently elevate serum lactate levels, including non-malarial sepsis, chronic liver disease, chronic kidney disease, diabetic ketoacidosis, or malignancy, pregnant women and patients receiving prior treatment that could significantly influence serum lactate levels before admission were excluded from study.

Diagnosis and species identification

Malaria diagnosis was established using peripheral blood smear examination and/or rapid diagnostic tests. Species identification was performed to classify infections as *P. falciparum*, *P. vivax*, or mixed infection.

Assessment of disease severity

Disease severity was classified according to the WHO criteria for severe malaria.[1,2] Patients presenting with one or more WHO-defined severity features-such as impaired consciousness, severe anemia (hemoglobin <7 g/dL), metabolic acidosis, hypoglycemia, acute kidney injury, jaundice with organ dysfunction, shock, or other evidence of organ dysfunction-were categorized as having severe malaria. Remaining patients were classified as having uncomplicated malaria.

Clinical and laboratory evaluation

Baseline clinical evaluation included documentation of demographic data, presenting symptoms, vital signs, and physical examination findings. Laboratory investigations included complete blood count, liver and renal function tests, blood glucose estimation, and other relevant investigations as clinically indicated.

Serum lactate estimation

Serum lactate levels were measured at the time of admission using standard enzymatic methods in the hospital laboratory. Sample collection and processing were performed according to standard protocols to minimize pre-analytical variability.

Outcome measures

Clinical outcomes were categorized as favorable or adverse. Adverse outcomes included intensive care unit (ICU) admission, prolonged hospital stay, or in-hospital mortality.

Statistical analysis

Data were entered into Microsoft excel and analyzed using SPSS software. Continuous variables were expressed as

mean±standard deviation, and categorical variables as frequencies and percentages. Comparison of mean serum lactate levels between groups was performed using an unpaired t-test with Welch's correction. A $p<0.05$ was considered statistically significant.

Ethical considerations

The study was approved by the institutional ethics committee of tertiary care hospital, Delhi. Written informed consent was obtained from all participants, and patient confidentiality was maintained throughout the study.

RESULTS

A total of 100 adult patients with laboratory-confirmed malaria were included in the study. All enrolled patients completed the study protocol and were included in the final analysis.

Baseline demographic characteristics

The majority of patients were young adults. The most common age groups were 20-29 years (41%) and 30-39 years (34%), followed by 40-49 years (12.9%), 13-19 years (6%), 50-59 years (5%), and 60-69 years (1%). There was a male predominance, with 57% (n=57) males and 43% (n=43) females (Figure 1).

Species distribution

P. vivax infection was identified in 48% (n=48) of patients, *Plasmodium falciparum* infection in 42% (n=42) patients, and mixed infection in 10% (n=10) patients (Table 1).

Disease severity classification

Disease severity was classified according to the WHO criteria for severe malaria.[1,2] Based on these criteria, patients were categorized as having either uncomplicated malaria or severe malaria (Table 2).

Serum lactate levels according to disease severity

Serum lactate levels were measured at admission in all patients. Patients with uncomplicated malaria demonstrated near-normal serum lactate levels, with a mean value of 1.6±0.4 mmol/l.

In contrast, patients with severe malaria had markedly elevated serum lactate levels, with a mean value of 4.5±1.2 mmol/l (Table 2).

Association between serum lactate and disease severity

The difference in serum lactate levels between uncomplicated and severe malaria was statistically highly significant ($p<0.0001$).

Association with clinical severity parameters

Elevated serum lactate levels were observed in patients presenting with major clinical severity parameters, including hypotension, severe anemia, metabolic acidosis, renal dysfunction, altered sensorium, liver dysfunction, thrombocytopenia, and hypoglycemia, all of which are recognized features of severe malaria as per WHO definitions (Table 3).[1,2]

Clinical outcomes

Clinical outcomes were categorized as favorable or adverse. Adverse outcomes occurred in 45% of patients, including ICU admission in 22 patients, prolonged hospital stay in 18 patients, and mortality in 8 patients.

Patients with favorable outcomes had significantly lower serum lactate levels (1.6±0.4 mmol/l) compared to those with adverse outcomes (4.5±1.2 mmol/l). This difference was statistically highly significant ($p<0.0001$) (Table 4).

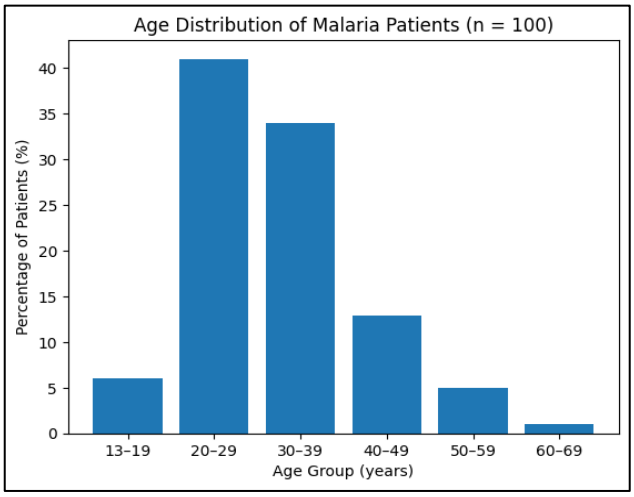

Figure 1: Age distribution of malaria patients, (n=100).

Table 1: Distribution of malaria species among study participants.

Malaria species	N	Percentage (%)
P. falciparum	42	42
P. vivax	48	48
Mixed infection	10	10
Total	100	100

Table 2: Serum lactate levels in relation to disease severity.

Disease severity	Serum lactate (mmol/L), mean±SD
Uncomplicated malaria	1.6±0.4 mmol/L
Severe malaria	4.5±1.2 mmol/L
P value	<0.0001

Table 3: Association of elevated serum lactate with clinical severity parameters.

Clinical parameters	Lactate level
Hypotension	↑
Severe anemia	↑
Metabolic acidosis	↑
Renal dysfunction	↑
Altered sensorium	↑
Liver dysfunction	↑
Thrombocytopenia	↑
Hypoglycemia	↑

Table 4: Serum lactate levels and clinical outcomes.

Outcomes	Serum lactate (mmol/l), mean±SD
Favorable outcome	1.6±0.4 mmol/l
Adverse outcome	4.5±1.2 mmol/l
P value	<0.0001

Adverse outcomes were ICU admission/prolonged hospitalization/complications.

DISCUSSION

The present prospective observational study evaluated the association between serum lactate levels, disease severity, and clinical outcomes in patients with malaria. The findings demonstrate a strong and statistically significant relationship between elevated serum lactate levels and severe malaria, multi-organ dysfunction, and adverse clinical outcomes, highlighting the prognostic value of serum lactate estimation in malaria.

In this study, patients with severe malaria had markedly higher serum lactate levels compared to those with uncomplicated disease (4.5±1.2 mmol/L vs 1.6±0.4 mmol/L; p<0.0001). This observation reflects the underlying pathophysiological mechanisms of severe malaria. Sequestration of parasitized erythrocytes within the microvasculature, endothelial dysfunction, and reduced red blood cell deformability result in impaired tissue perfusion and oxygen delivery, leading to tissue hypoxia and increased anaerobic metabolism with lactate accumulation.[4,7,10]

Hyperlactatemia has been recognized as a key marker of metabolic acidosis and disease severity in malaria. Previous studies have demonstrated that elevated serum lactate levels correlate strongly with metabolic acidosis, organ dysfunction, and mortality, particularly in severe *P. falciparum* infection.[4-6] Similar findings have been reported in both adult and pediatric populations, establishing serum lactate as a robust prognostic indicator in malaria.[5,6,9]

In the present study, elevated serum lactate levels were consistently associated with major clinical severity parameters, including hypotension, severe anemia, metabolic acidosis, renal dysfunction, altered sensorium, liver dysfunction, thrombocytopenia, and hypoglycemia. These associations suggest that hyperlactatemia serves as a global marker of systemic involvement and multi-organ dysfunction in malaria. In addition to increased lactate production due to tissue hypoxia, impaired hepatic clearance and heightened inflammatory responses may further contribute to elevated lactate levels in severe disease.[7,10]

A significant finding of this study is the strong association between serum lactate levels and adverse clinical outcomes. Adverse outcomes were observed in 45% of patients and included ICU admission (22%), prolonged hospital stay (18%), and mortality (8%). Patients with adverse outcomes demonstrated significantly higher serum lactate levels at presentation compared to those with favorable outcomes (4.5±1.2 mmol/L vs 1.6±0.4 mmol/L; p<0.0001). This finding is consistent with earlier studies, which have shown that elevated lactate levels are predictive of poor outcomes and mortality in malaria.[4-6,9]

The findings of the present study are in agreement with previous literature that has established hyperlactatemia as an important marker of disease severity and prognosis in malaria.[4-6,9,10] The present study adds to existing evidence by demonstrating these associations in an Indian tertiary care setting and by including both *P. falciparum* and *P. vivax* infections, thereby enhancing the generalizability of the findings. This is particularly relevant in the Indian context, where both species contribute significantly to malaria burden.[1-3,14]

From a clinical perspective, serum lactate estimation is a rapid, inexpensive, and widely available investigation that can be performed at the time of hospital admission.

The WHO emphasizes early recognition and prompt management of severe malaria to reduce mortality.[1,2] Incorporating serum lactate measurement into the initial evaluation of malaria patients may aid in early risk stratification, guide decisions regarding level of care, and facilitate timely escalation to intensive management, potentially improving patient outcomes.

Table 5: Comparison of serum lactate levels and outcomes in malaria: present study vs previous studies.

Study	Study population	Lactate in uncomplicated malaria (mmol/L)	Lactate in severe malaria (mmol/L)	Key outcome association	Study	Study population
Present study	Adults, India (n=100)	1.6±0.4	4.5±1.2	Strong association with severity, ICU admission, and mortality	Present study	Adults, India, (n=100)

Continued.

Study	Study population	Lactate in uncomplicated malaria (mmol/L)	Lactate in severe malaria (mmol/L)	Key outcome association	Study	Study population
Day et al 2000	Adults, Vietnam	~1.8	~5.0	Prognostic marker for severity and mortality	Day et al 2000	Adults, Vietnam
English et al 1997	Children, Africa	~2.0	~6.2	Strong predictor of fatal outcome	English et al 1997	Children, Africa
Krishna et al 1994	Children, severe malaria	-	>4.0	Associated with hypoglycemia and mortality	Krishna et al 1994	Children, severe malaria
van Genderen et al 2005	Adult travelers	~1.5–2.0	>4.0	Correlated with disease severity at admission	van Genderen et al 2005	Adult travelers

Future directions

Future multicentric studies with larger sample sizes and serial lactate monitoring are warranted to validate these findings. Further research may also explore the role of lactate clearance as a prognostic marker and its integration into severity assessment and management algorithms for malaria.

Limitations

This study has certain limitations. Being a single-center observational study, the findings may not be generalizable to all populations. Serial lactate measurements were not performed, which could have provided insight into lactate clearance and dynamic response to therapy. Additionally, long-term follow-up outcomes were not assessed.

CONCLUSION

Serum lactate levels are significantly elevated in patients with severe malaria and show a strong association with disease severity, multi-organ dysfunction, and adverse clinical outcomes. Elevated serum lactate at presentation is a valuable prognostic marker for identifying high-risk patients, including those requiring intensive care and those at increased risk of mortality. Early estimation of serum lactate may aid in prompt risk stratification, closer monitoring, and timely escalation of care, thereby potentially improving clinical outcomes in patients with malaria.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mehta B, Lal D, Behera N, Vekariya G. Serum lactate levels as a marker of clinical severity in malaria: a prospective observational study. Int J Res Med Sci 2026;14:3352-7.