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Original Research Article

Outcome determinants in pediatric severe malaria: evidence from a tertiary care hospital in Odisha

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ABSTRACT

Background: The objectives of the study were to assess socio-demographic, clinical, and laboratory predictors of outcomes in pediatric patients with severe malaria, focusing on sex-based differences and complication profiles.
Methods: A cross-sectional study was conducted among 102 children aged 0–14 years with confirmed severe malaria admitted to a tertiary care hospital. Data on socio-demographic characteristics, clinical features, and laboratory abnormalities were collected. Outcomes were categorized as treated, referred, or deceased. Associations between variables and outcomes were analyzed using the Chi-square test, with Cramer's V for effect size. A p value <0.05 was considered statistically significant.
Results: Most participants were aged 5–10 years (47.1%), female (58.8%), from rural areas (76.5%), and of upper-lower socio-economic class (86.3%). The most frequent complications were severe anemia with prostration (29.4%), prostration alone (25.5%), and renal failure with prostration (15.7%). Overall, 80.4% were successfully treated, 11.8% referred, and 7.8% died. Sex showed a significant association with outcome (χ^2=15.619, p<0.001, Cramer's V=0.39), with males having higher mortality (14.3% versus 3.3%) and referral rates (23.8% versus 3.3%), while females had better treatment success (93.3% versus 61.9%). Laboratory complications were also strongly associated with outcomes (χ^2=121.046, p<0.001), with multi-organ dysfunction predicting fatality and isolated prostration linked to recovery. Socio-economic status (p=0.412) and age group (p=0.179) showed no significant association.
Conclusion: Male sex and severe laboratory abnormalities are key predictors of adverse outcomes in pediatric severe malaria. Early identification of high-risk patients through sex-specific and laboratory-based risk stratification may improve clinical management and survival rates.

Keywords: Anemia, Child, Malaria, Prognosis, Sex factors

INTRODUCTION

Malaria remains a leading cause of morbidity and mortality among children worldwide, with those under five years of age at greatest risk for severe disease and death.[1] Severe malaria, most often due to *Plasmodium falciparum*, is characterized by complications such as cerebral involvement, severe anemia, metabolic acidosis, respiratory distress, and multi-organ dysfunction, each associated with high fatality rates if not promptly treated.[2-4] Globally, despite large-scale prevention and treatment programs reducing malaria cases and deaths since 2000, the disease continues to cause an estimated 263 million cases and 597,000 deaths annually, with 95% occurring in the African region.[1,5] India has recorded a 69% reduction in malaria cases and a 68% decline in malaria-related deaths between 2017 and 2023, aided by artemisinin-based combination therapy, long-lasting insecticidal nets, indoor residual spraying, and targeted community-level interventions.[6-8] Nevertheless, high-burden pockets persist, particularly in tribal and forested districts, where children frequently present with severe complications and require hospital admission.[9,10]

In high-endemic regions, tertiary care centers play a crucial role in managing the most critical pediatric cases referred from peripheral facilities. However, data from such referral hospitals are scarce, particularly on how socio-demographic factors, clinical features, and laboratory abnormalities influence patient outcomes.

Preliminary reports from endemic districts suggest that neurological manifestations, respiratory distress, and severe anemia are common presentations in pediatric severe malaria, but sex-based differences in outcomes and complication-specific prognoses remain poorly understood.[11,12]

This study was designed to address this gap by systematically assessing socio-demographic, clinical, and laboratory predictors of outcomes in children with severe malaria at a tertiary care hospital in an endemic district of Odisha, with a specific focus on sex-based differences and complication profiles. The findings aim to inform risk stratification, guide early referral, and improve survival rates in similar high-burden settings.

METHODS

This was a hospital-based cross-sectional study conducted in the Department of Pediatrics at a tertiary care hospital. This hospital caters to both rural and semi-urban populations, including a large tribal catchment area with high malaria endemicity.

The study was conducted over a 6-month period from June 2024 to November 2024, encompassing both the monsoon and post-monsoon seasons, which correspond to the peak malaria transmission period in the region. The study population comprised children aged 0–14 years presenting with fever and diagnosed with severe malaria according to World Health Organization (WHO) criteria.

Inclusion criteria

The inclusion criteria for the study were children aged 0–14 years admitted with fever; laboratory confirmation of Plasmodium falciparum or mixed infection by peripheral smear or rapid diagnostic test (RDT); fulfilment of WHO clinical and/or laboratory criteria for severe malaria, such as cerebral malaria, severe anemia, respiratory distress, metabolic acidosis, renal failure, jaundice, prostration, shock, abnormal bleeding, pulmonary edema, or hypoglycemia; and patients (or parents/legal guardians in the case of minors) who were willing to participate and provided written informed consent.

Exclusion criteria

The exclusion criteria were children with confirmed alternative causes of severe febrile illness, such as bacterial meningitis, septicemia, dengue, or scrub typhus; and children with incomplete clinical or laboratory records.

For a cross-sectional study estimating a proportion we used the standard formula, where, n=required sample size, Z=value for desired confidence level (1.96 for 95% CI), p=anticipated proportion (prevalence) of the primary outcome, d=desired absolute precision (margin of error), confidence level=95% → Z=1.96, anticipated proportion=50% → p=0.50, and margin of error=10% → d=0.10.

$$n = (Z^2 \times p \times (1 - p))/d^2$$

The calculated sample size after adjustment was 102. All eligible consecutive cases meeting the inclusion criteria during the study period were enrolled until the sample target of 102 was reached.

A convenience (consecutive) sampling approach was used, all children aged 0–14 years admitted with fever who met the inclusion criteria and whose parents/legal guardians provided written informed consent during the study period (June 2024–November 2024) were included consecutively until the sample of 100 participants was achieved. Data were collected using a structured proforma designed for the study, which included the following sections.

Demographic details

Age group (0–5 years, 5–10 years, 11–14 years), sex, place of residence (urban, semi-urban, rural), religion, socioeconomic indicators (education and occupation of head of family, per capita monthly family income as per modified Kuppuswamy socioeconomic scale).[13-15]

Clinical details

History of previous malaria infection, month of admission, presenting symptoms (coma, altered consciousness, convulsions, respiratory distress, jaundice, none).

Laboratory parameters

Hemoglobin levels, blood glucose, renal function tests, acid–base status, coagulation profile, and chest radiography where indicated.

Severe malaria criteria (WHO)

Severe anemia (Hb <5 g/dl for children <12 years or Hb <7 g/dl for children >12 years), hypoglycemia (<40 mg/dl), renal failure (creatinine >3 mg/dl or blood urea >20 mmol/l), prostration, shock (systolic BP <70 mmHg in children), pulmonary edema (radiological), abnormal bleeding, metabolic acidosis (base deficit >8 mEq/l or plasma bicarbonate <15 mmol/l or venous plasma lactate >5 mmol/l).[16]

Outcome

The participants were treated and discharged, referred, or declared dead.

Parents or legal guardians provided written informed consent before enrolment. All ethical principles outlined in the Declaration of Helsinki were followed. Severe malaria was defined according to WHO 2022 guidelines based on the presence of one or more life-threatening clinical or laboratory features in a patient with confirmed malaria infection.[17,18]

Data were entered into Microsoft Excel and analyzed using statistical package for the social sciences (SPSS) software version 27.0.1 (IBM Corp., Armonk, NY, USA).[19] Categorical variables were expressed as frequencies and percentages. Continuous variables were summarized using mean±standard deviation (SD) or median (interquartile range) as appropriate. Associations between categorical variables were tested using the Chi-square test or Fisher's exact test. A p value <0.05 was considered statistically significant.

All participant data were anonymized and kept confidential. The study results may be used for academic publication purposes without revealing individual identities.

RESULTS

A total of 102 pediatric patients with confirmed severe malaria were included. The majority (86.3%) belonged to the upper lower socio-economic class, followed by lower middle (9.8%) and lower (3.9%) classes. Most children were aged 5–10 years (47.1%), followed by 0–5 years (37.3%) and 11–14 years (15.7%). Females comprised 58.8% of the participants.

Most patients resided in rural areas (76.5%), followed by semi-urban (21.6%) and urban (2.0%) areas. The predominant religion was Hinduism (74.5%), followed by Christianity (15.7%) and Islam (9.8%). A previous history of malaria was present in 13.7% of cases. The most common clinical features at presentation included altered consciousness (19.6%), jaundice (11.8%), respiratory distress (11.8%), and convulsions with altered consciousness (9.8%). Among laboratory abnormalities, severe anemia with prostration was most frequent (29.4%), followed by prostration alone (25.5%) and renal failure with prostration (15.7%) (Table 1).

Of the total patients, 80.4% were successfully treated, 11.8% were referred to higher centers, and 7.8% died during hospitalization (Figure 1).

Table 1: Socio-demographic and clinical characteristics of the study participants (n=102).

Variables	N (%)
Socio-economic class	
Upper lower	88 (86.3)
Lower middle	10 (9.8)
Lower	4 (3.9)
Age group (years)	
0–5	38 (37.3)
5–10	48 (47.1)
11–14	16 (15.7)
Sex	
Female	60 (58.8)
Male	42 (41.2)
Residency	
Rural	78 (76.5)
Semi-urban	22 (21.6)
Urban	2 (2.0)
Religion	
Hindu	76 (74.5)
Christian	16 (15.7)
Muslim	10 (9.8)
Previous malaria	
Yes	14 (13.7)
No	88 (86.3)
Common clinical features	
Altered consciousness	20 (19.6)
Jaundice	12 (11.8)
Respiratory distress	12 (11.8)
Convulsions + altered consciousness	10 (9.8)
Common lab findings	
Severe anemia + prostration	30 (29.4)
Prostration alone	26 (25.5)
Renal failure + prostration	16 (15.7)

Table 2 demonstrates significant sex-based disparities in malaria outcomes (χ^2=15.619, p<0.001). Male patients exhibited substantially higher mortality (14.3% versus 3.3%) and referral rates (23.8% versus 3.3%), while female patients achieved superior treatment success (93.3% versus 61.9%). These findings, supported by a large effect size (Cramer's V=0.39), underscore the critical importance of sex as a prognostic indicator in severe malaria management, suggesting male pediatric patients may require more intensive clinical monitoring and earlier intervention strategies.

Table 2: Association between sex and treatment outcomes with statistical test results.

Sex	Death (%)	Referred (%)	Treated (%)	Total (n)	χ^2 (P value)
Male	14.3	23.8	61.9	42	χ^2=15.619 (p<0.001)
Female	3.3	3.3	93.3	60	
Total	7.8	11.8	80.4	102	

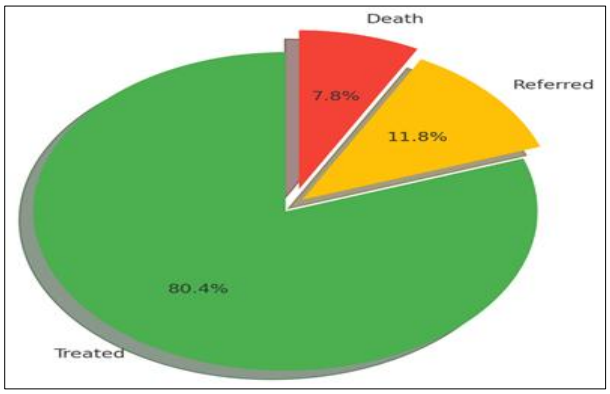

Figure 1: Distribution of outcomes among study participants.

Table 3 reveals distinct complication patterns by outcomes; multi-organ failure (50% of deaths) was exclusively fatal, while renal failure with prostration (33.3%) prompted more referrals. Isolated prostration (31.7%) correlated with successful treatment, suggesting it's a manageable presentation. These findings (χ^2=121.046, p<0.001) highlight the prognostic value of laboratory markers in severe malaria.

Table 4 shows sex (χ^2=15.619, p<0.001) and laboratory complications (χ^2=121.046, p<0.001) significantly predicted outcomes, while socio-economic status (p=0.412) and age (p=0.179) did not. These results highlight the critical prognostic value of clinical and biological factors over demographic characteristics in severe malaria management.

Table 3: Key laboratory findings associated with outcome.

Complication	Death (n=8)	Referred (n=12)	Treated (n=82)
Severe anemia + renal failure + metabolic acidosis + shock	4 (50.0)	0	0
Severe anemia + prostration	2 (25.0)	2 (16.7)	26 (31.7)
Renal failure + prostration	0	4 (33.3)	12 (14.6)
Prostration alone	0	0	26 (31.7)

Table 4: Association between socio-demographic/laboratory variables and outcome.

Variable	χ^2 value	P value
Sex	15.619	<0.001*
Laboratory complications	121.046	<0.001*
Socio-economic class	1.771	0.412
Age group	3.446	0.179

*P value statistically significant

DISCUSSION

In our cohort of 102 pediatric patients with severe malaria at a tertiary care center in Baripada, Odisha, male sex and the presence of multi-organ laboratory complications emerged as powerful predictors of adverse outcomes. Socio-economic status and age did not significantly influence mortality.

Our finding that multi-organ dysfunction significantly predicts fatal outcomes aligns with earlier observational data from Orissa by Tripathy et al, who identified respiratory distress, coma, and multi-organ involvement as major determinants of mortality in pediatric severe malaria (case fatality ~12%).[20] Similarly, a more recent study from Berhampur, Odisha, demonstrated that case fatality rates rose proportionally with the number of organs involved particularly when four to five systems were compromised (up to 100% mortality). These findings underscore the critical prognostic relevance of thorough multi-system assessment.

We observed significantly worse outcomes among male children (mortality 14.3% versus 3.3%, p<0.001). While some pediatric studies report no such sex differential (McDonald et al in Uganda and Mohanty et al), broader clinical evidence supports the concept of sex-based immunological differences, with females generally mounting more robust resistance to infectious diseases.[21,22] This is partly attributed to hormonal influences, such as the immunoprotective effects of estradiol compared to the immunosuppressive effects of testosterone, as described in Takahashi et al.[23]

Expanding understanding of host response, Briggs et al demonstrated that in a Ugandan cohort, females cleared chronic, asymptomatic *P. falciparum* infections nearly twice as fast as males (hazard ratios ~2.0), even after adjusting for age and parasite density, implying inherent sex-linked biological differences in malaria immunity.[24] This complements our clinical findings of worse outcomes in male children. Complementary epidemiological evidence supports sex-specific variations in immune responses, such as higher HMGB1 protein concentrations and differential monocyte activity in males with malaria, suggesting varied inflammatory responses may underpin observed clinical differences.[25]

The factors identified in our study reaffirm the critical importance of both clinical severity and biological sex in determining pediatric malaria outcomes. While socio-demographic factors like socio-economic status and age are important at the population level, in-hospital outcomes appear more strongly tied to clinical presentation and physiological responses.

This study's strengths include detailed characterization of complication profiles in a high-burden, under-studied region. Limitations include its single-center design,

modest sample size especially limited number of deaths and lack of data on the timing of admission, nutritional status, or access to pre-hospital care.

Implications for practice and future research

Clinical management

Pediatric severe malaria protocols should prioritize rapid risk stratification based on clinical severity and consider male children particularly those with multi-organ involvement for heightened monitoring, early intensive care resuscitation, and prompt referral.

Research directions

Larger, multicenter studies are needed to validate the observed sex-based disparities, ideally incorporating immunological biomarkers to elucidate underlying mechanisms.

Policy and public health

Strengthening pre-hospital referral systems and expanding training in early identification of high-risk presentations would be especially valuable in forested, tribal regions like Mayurbhanj.

CONCLUSION

This study demonstrates that in pediatric severe malaria, sex and laboratory complications are key prognostic determinants, while socio-economic status and age show no significant association with outcomes. Male children experienced higher mortality and referral rates, whereas females had better treatment success. Multi-organ dysfunction, particularly when involving severe anemia, renal failure, metabolic acidosis, and shock, was strongly predictive of fatal outcomes. These findings highlight the importance of early identification of high-risk patients especially males and those with severe laboratory abnormalities to facilitate timely referral, intensive monitoring, and targeted interventions. Integrating sex-specific risk stratification and laboratory-based prognostic assessment into clinical protocols could improve survival and reduce morbidity in pediatric severe malaria.

Recommendations

Male pediatric patients with severe malaria face significantly higher mortality and referral rates compared to females, underscoring sex as an important prognostic factor. Multi-organ failure, especially when involving severe anemia, renal failure, metabolic acidosis, and shock, is strongly linked to fatal outcomes and requires urgent aggressive management. Isolated prostration is associated with favorable recovery, suggesting it is a comparatively manageable presentation of severe malaria. Socio-economic status and age group do not significantly influence treatment outcomes, highlighting the overriding importance of clinical and laboratory parameters. Early identification of high-risk patients using sex-specific risk stratification and laboratory markers can guide timely, targeted interventions to improve survival in pediatric severe malaria.

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