



## The Great Mimicker: Predictors of Mortality in Scrub Typhus.

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**Received:** 04-04-2026

**Revised:** 20-05-2026

**Accepted:** 03-06-2026

**Published:** 18-07-2026

### Abstract

**Background:** Scrub typhus is an important re-emerging zoonotic infection and a major cause of acute undifferentiated febrile illness in tropical countries. Owing to its diverse clinical manifestations and potential for rapid progression to multiorgan dysfunction, it is often referred to as the "great mimicker." Early identification of patients at risk of adverse outcomes is essential for timely intervention. The present study aimed to evaluate the demographic, clinical, and laboratory characteristics of patients with scrub typhus and identify independent predictors of in-hospital mortality. **Materials and Methods:** A hospital-based retrospective observational study was conducted among 90 adult patients with laboratory-confirmed scrub typhus admitted to a tertiary care teaching hospital between January 2025 to January 2026. Demographic details, clinical features, laboratory parameters, complications, intensive care requirements, and treatment outcomes were retrieved from medical records. Patients were categorized into survivors and non-survivors. Comparative analyses were performed using appropriate statistical tests, followed by univariate and multivariate logistic regression to identify independent predictors of mortality. **Results:** Among the 90 patients, 76 (84.4%) survived and 14 (15.6%) died during hospitalization. Fever was present in all patients, while headache, myalgia, and chills were the most common presenting symptoms. Hepatitis (46.7%), thrombocytopenia (43.3%), and acute kidney injury (26.7%) were the predominant complications. Compared with survivors, non-survivors were significantly older and more frequently had altered sensorium, hypotension, acute kidney injury, acute respiratory distress syndrome (ARDS), septic shock, and multiple organ dysfunction syndrome (all  $p < 0.05$ ). Multivariate logistic regression identified altered sensorium, hypotension, acute kidney injury, ARDS, multiple organ dysfunction syndrome, and elevated serum creatinine as independent predictors of mortality. ROC analysis demonstrated excellent predictive performance of serum creatinine (AUC=0.891), followed by C-reactive protein, serum albumin, platelet count, and serum bilirubin. **Conclusion:** Scrub typhus is associated with considerable morbidity and mortality due to multiorgan involvement. Early recognition of high-risk clinical features and readily available laboratory markers can facilitate prompt risk stratification, timely intensive care management, and improved patient outcomes.

**Keywords:** Scrub typhus; Mortality; Acute kidney injury; Acute respiratory distress syndrome; Predictors.



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### INTRODUCTION

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi*, an obligate intracellular gram-negative bacterium transmitted to humans through the bite of infected larval trombiculid mites (chiggers) [1]. The disease is endemic throughout the "tsutsugamushi triangle," which includes India and several countries in Southeast Asia and the Western Pacific [2]. In recent years, scrub typhus has re-emerged as a significant public health concern in India, contributing substantially to cases of acute undifferentiated febrile illness, particularly during the post-monsoon and cooler months [3]. Despite its widespread occurrence, the disease often remains underdiagnosed because of its nonspecific clinical manifestations and limited awareness among healthcare providers [4].

Scrub typhus has long been recognized as the "great mimicker" because its clinical presentation closely resembles that of several tropical infections, including dengue, malaria, leptospirosis, typhoid fever, and viral hemorrhagic fevers [5]. Patients commonly present with fever, headache, myalgia, gastrointestinal symptoms, cough, or rash, while the characteristic eschar is absent in a substantial proportion of cases [6]. The broad spectrum of clinical manifestations frequently delays diagnosis and initiation of appropriate antimicrobial therapy [7]. If left untreated, scrub typhus can rapidly progress to severe multisystem involvement, resulting in complications such as acute respiratory distress syndrome

(ARDS), acute kidney injury (AKI), hepatitis, myocarditis, meningoencephalitis, septic shock, and multiple organ dysfunction syndrome (MODS), all of which contribute to increased mortality [8].

Early diagnosis and prompt initiation of doxycycline or azithromycin have dramatically improved clinical outcomes; however, mortality remains considerable among patients presenting with severe disease or delayed treatment [9]. Several studies have identified advanced age, hypotension, altered sensorium, thrombocytopenia, elevated liver enzymes, renal dysfunction, hyperbilirubinemia, and organ failure as potential predictors of poor prognosis [10]. Nevertheless, the relative contribution of these factors varies across different geographical regions and healthcare settings because of differences in patient characteristics, circulating strains, healthcare accessibility, and timing of presentation. Consequently, identification of locally relevant predictors of mortality is essential for early risk stratification, timely referral to intensive care, and optimal resource utilization. The present study aimed to evaluate the demographic, clinical, and laboratory characteristics of patients with scrub typhus and to identify independent predictors of in-hospital mortality among patients admitted to a tertiary care teaching hospital.

## **MATERIALS AND METHODS**

This hospital-based retrospective observational study was conducted in the Department of General Medicine at a tertiary care teaching hospital over a one-year period from January 2025 to January 2026. The study included 90 consecutive adult patients diagnosed with scrub typhus who fulfilled the predefined eligibility criteria. Diagnosis was established based on compatible clinical features along with laboratory confirmation using a positive scrub typhus IgM enzyme-linked immunosorbent assay (ELISA) and/or other standard institutional diagnostic methods. Patients aged 18 years or older with complete medical records were included, whereas patients with incomplete records, coinfections (such as dengue, malaria, leptospirosis, or enteric fever), or pre-existing terminal illnesses that could independently influence mortality were excluded from the analysis. Approval from the Institutional Ethics Committee was obtained before commencement of the study. Demographic details including age, sex, residence, duration of fever, and underlying comorbidities were retrieved from hospital records. Clinical information comprising presenting symptoms (fever, headache, myalgia, vomiting, abdominal pain, cough, dyspnea, altered sensorium, rash, and eschar) and physical examination findings (hepatomegaly, splenomegaly, lymphadenopathy, and hypotension) was documented. Laboratory investigations recorded at admission included complete blood count, liver function tests, renal function tests, serum electrolytes, C-reactive protein (CRP), and serum albumin. Patients were monitored throughout hospitalization for the development of complications including acute kidney injury (AKI), hepatitis, thrombocytopenia, acute respiratory distress syndrome (ARDS), septic shock, myocarditis, meningoencephalitis, and multiple organ dysfunction syndrome (MODS). Details regarding intensive care unit (ICU) admission, requirement for mechanical ventilation, duration of hospital stay, and final outcome (survival or death) were also collected.

The primary outcome of the study was in-hospital mortality. Patients were categorized into survivors and non-survivors, and demographic, clinical, laboratory, and complication-related variables were compared between the two groups to identify factors associated with mortality. Variables showing significant associations on initial analysis were further evaluated to determine independent predictors of mortality. Receiver operating characteristic (ROC) curve analysis was also performed for selected continuous variables to assess their ability to predict mortality and to identify optimal diagnostic cut-off values.

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software version 20 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean  $\pm$  standard deviation (SD) or median with interquartile range (IQR), depending on data distribution, while categorical variables were presented as frequencies and percentages. Comparisons between survivors and non-survivors were performed using the independent Student's t-test or Mann-Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. Variables with statistical significance on univariate analysis were entered into a multivariate logistic regression model to identify independent predictors of mortality. Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive performance of significant laboratory parameters. A two-tailed p value of  $<0.05$  was considered statistically significant throughout the analysis.

## **RESULTS**

A total of 90 patients with confirmed scrub typhus were included in the study. The largest proportion belonged to the 31–40 years age group (24.4%), followed by 41–50 years (23.3%). The mean age of the cohort was predominantly middle-aged, and males constituted 56.7% of the study population. Most participants were from rural areas (67.8%). Hypertension (28.9%) and diabetes mellitus (23.3%) were the most common comorbidities, while over half of the patients (51.1%) had no underlying comorbid illness. Fever duration of  $\leq 7$  days before admission was observed in 64.4% of patients. (Table 1)

**Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants (N = 90)**

| Variable               | Category | n (%)     |
|------------------------|----------|-----------|
| Age (years)            | 18–30    | 17 (18.9) |
|                        | 31–40    | 22 (24.4) |
|                        | 41–50    | 21 (23.3) |
|                        | 51–60    | 18 (20.0) |
|                        | >60      | 12 (13.3) |
| Gender                 | Male     | 51 (56.7) |
|                        | Female   | 39 (43.3) |
| Residence              | Rural    | 61 (67.8) |
|                        | Urban    | 29 (32.2) |
| Diabetes mellitus      | Yes      | 21 (23.3) |
| Hypertension           | Yes      | 26 (28.9) |
| Chronic kidney disease | Yes      | 6 (6.7)   |
| Chronic liver disease  | Yes      | 4 (4.4)   |
| No comorbidity         | Yes      | 46 (51.1) |
| Duration of fever      | ≤7 days  | 58 (64.4) |
|                        | >7 days  | 32 (35.6) |

Fever was present in all patients (100%). The most common accompanying symptoms were headache (71.1%), myalgia (67.8%), chills (62.2%), and vomiting (37.8%). Respiratory symptoms such as cough (31.1%) and dyspnea (26.7%) were also frequent. Eschar, the characteristic lesion of scrub typhus, was identified in 30.0% of patients, while hepatomegaly, splenomegaly, and lymphadenopathy were observed in 25.6%, 18.9%, and 14.4% of cases, respectively. (Table 2)

**Table 2. Clinical Presentation at Admission (N = 90)**

| Clinical feature  | n (%)      |
|-------------------|------------|
| Fever             | 90 (100.0) |
| Headache          | 64 (71.1)  |
| Myalgia           | 61 (67.8)  |
| Chills            | 56 (62.2)  |
| Vomiting          | 34 (37.8)  |
| Abdominal pain    | 29 (32.2)  |
| Cough             | 28 (31.1)  |
| Dyspnea           | 24 (26.7)  |
| Altered sensorium | 14 (15.6)  |
| Rash              | 18 (20.0)  |
| Eschar            | 27 (30.0)  |
| Hepatomegaly      | 23 (25.6)  |
| Splenomegaly      | 17 (18.9)  |
| Lymphadenopathy   | 13 (14.4)  |
| Hypotension       | 16 (17.8)  |

The mean hemoglobin level was  $10.8 \pm 2.1$  g/dL, while the average total leukocyte count was  $11,940 \pm 5,420/\text{mm}^3$ . Patients demonstrated thrombocytopenia with a mean platelet count of  $118 \pm 62 \times 10^3/\mu\text{L}$ . Elevated liver enzymes, bilirubin, inflammatory markers, and serum creatinine indicated significant hepatic, renal, and systemic inflammatory involvement. The mean serum albumin was reduced to  $3.01 \pm 0.69$  g/dL, reflecting disease severity. (Table 3)

**Table 3. Laboratory Parameters at Admission**

| Parameter                                    | Mean $\pm$ SD      |
|----------------------------------------------|--------------------|
| Hemoglobin (g/dL)                            | $10.8 \pm 2.1$     |
| Total leukocyte count ( $/\text{mm}^3$ )     | $11,940 \pm 5,420$ |
| Platelet count ( $\times 10^3/\mu\text{L}$ ) | $118 \pm 62$       |
| Serum creatinine (mg/dL)                     | $1.69 \pm 1.18$    |
| Total bilirubin (mg/dL)                      | $2.31 \pm 1.64$    |
| AST (IU/L)                                   | $165 \pm 98$       |
| ALT (IU/L)                                   | $138 \pm 82$       |
| Serum albumin (g/dL)                         | $3.01 \pm 0.69$    |
| CRP (mg/L)                                   | $88 \pm 46$        |
| Sodium (mEq/L)                               | $132 \pm 5.9$      |

Hepatitis was the most common complication, affecting 46.7% of patients, followed by thrombocytopenia (43.3%) and acute kidney injury (26.7%). Acute respiratory distress syndrome (17.8%), septic shock (14.4%), and multiple organ dysfunction syndrome (13.3%) were among the major life-threatening complications. Nearly one-fifth of patients required ICU admission (21.1%), while 16.7% required mechanical ventilation. (Table 4)

**Table 4. Organ Dysfunction and Complications During Hospital Stay**

| Complication                | n (%)     |
|-----------------------------|-----------|
| Acute kidney injury         | 24 (26.7) |
| Hepatitis                   | 42 (46.7) |
| Thrombocytopenia (<100,000) | 39 (43.3) |
| ARDS                        | 16 (17.8) |
| Septic shock                | 13 (14.4) |
| Meningoencephalitis         | 8 (8.9)   |
| Myocarditis                 | 6 (6.7)   |
| MODS                        | 12 (13.3) |
| ICU admission               | 19 (21.1) |
| Mechanical ventilation      | 15 (16.7) |

Among the 90 patients, 76 (84.4%) survived and 14 (15.6%) died during hospitalization. The median duration of hospital stay was 8 days (IQR: 6–11 days). ICU admission was required in 21.1% of patients, whereas mechanical ventilatory support was needed in 16.7%, reflecting the burden of severe disease in a subset of patients. (Table 5)

**Table 5. Hospital Outcomes**

| Outcome                     | n (%)        |
|-----------------------------|--------------|
| Survived                    | 76 (84.4)    |
| Died                        | 14 (15.6)    |
| Median hospital stay (days) | 8 (IQR 6–11) |
| ICU stay                    | 19 (21.1)    |
| Mechanical ventilation      | 15 (16.7)    |

Compared with survivors, non-survivors were significantly older and had a higher prevalence of diabetes mellitus and hypertension. Altered sensorium, hypotension, acute kidney injury, ARDS, septic shock, and multiple organ dysfunction syndrome were significantly more common among non-survivors (all  $p < 0.05$ ). Non-survivors also demonstrated significantly lower platelet counts and serum albumin levels, along with markedly higher serum creatinine, bilirubin, AST, and CRP values, indicating greater disease severity. (Table 6)

**Table 6. Comparison Between Survivors and Non-survivors**

| Variable                                     | Survivors (n=76) | Non-survivors (n=14) | p value |
|----------------------------------------------|------------------|----------------------|---------|
| Mean age (years)                             | 43.6 ± 15.2      | 59.7 ± 13.4          | <0.001  |
| Male sex                                     | 41 (53.9)        | 10 (71.4)            | 0.233   |
| Diabetes                                     | 15 (19.7)        | 6 (42.9)             | 0.048   |
| Hypertension                                 | 19 (25.0)        | 7 (50.0)             | 0.046   |
| Eschar                                       | 25 (32.9)        | 2 (14.3)             | 0.184   |
| Altered sensorium                            | 7 (9.2)          | 7 (50.0)             | <0.001  |
| Hypotension                                  | 8 (10.5)         | 8 (57.1)             | <0.001  |
| Platelet count ( $\times 10^3/\mu\text{L}$ ) | 128 ± 58         | 67 ± 31              | <0.001  |
| Creatinine (mg/dL)                           | 1.34 ± 0.88      | 3.18 ± 1.61          | <0.001  |
| Bilirubin (mg/dL)                            | 1.96 ± 1.22      | 4.24 ± 2.11          | <0.001  |
| AST (IU/L)                                   | 146 ± 84         | 268 ± 102            | <0.001  |
| Albumin (g/dL)                               | 3.15 ± 0.56      | 2.29 ± 0.47          | <0.001  |
| CRP (mg/L)                                   | 79 ± 39          | 137 ± 48             | <0.001  |
| ARDS                                         | 6 (7.9)          | 10 (71.4)            | <0.001  |
| AKI                                          | 15 (19.7)        | 9 (64.3)             | <0.001  |
| Septic shock                                 | 3 (3.9)          | 10 (71.4)            | <0.001  |
| MODS                                         | 2 (2.6)          | 10 (71.4)            | <0.001  |

On univariate logistic regression analysis, older age, diabetes mellitus, hypertension, altered sensorium, hypotension, thrombocytopenia, elevated serum creatinine, hyperbilirubinemia, acute kidney injury, ARDS, septic shock, and multiple organ dysfunction syndrome were significantly associated with increased odds of mortality. Multiple organ dysfunction syndrome and septic shock exhibited the strongest associations with mortality. (Table 7)

**Table 7. Univariate Logistic Regression Analysis for Mortality**

| Variable                                | Odds Ratio | 95% CI      | p value |
|-----------------------------------------|------------|-------------|---------|
| Age >60 years                           | 4.12       | 1.46–11.58  | 0.007   |
| Diabetes mellitus                       | 3.03       | 1.01–9.11   | 0.048   |
| Hypertension                            | 3.00       | 1.02–8.86   | 0.046   |
| Altered sensorium                       | 9.90       | 2.73–35.90  | <0.001  |
| Hypotension                             | 11.31      | 3.23–39.57  | <0.001  |
| AKI                                     | 7.31       | 2.23–23.91  | <0.001  |
| ARDS                                    | 28.92      | 7.06–118.4  | <0.001  |
| Septic shock                            | 61.67      | 11.59–327.8 | <0.001  |
| MODS                                    | 92.50      | 15.82–541.2 | <0.001  |
| Platelet count <100×10 <sup>3</sup> /μL | 5.02       | 1.64–15.38  | 0.005   |
| Creatinine >2 mg/dL                     | 8.44       | 2.54–28.08  | <0.001  |
| Bilirubin >3 mg/dL                      | 5.91       | 1.88–18.55  | 0.002   |

Multivariate logistic regression identified altered sensorium, hypotension, acute kidney injury, ARDS, multiple organ dysfunction syndrome, and elevated serum creatinine as independent predictors of in-hospital mortality after adjusting for potential confounding variables. Among these, multiple organ dysfunction syndrome demonstrated the highest adjusted odds of mortality, followed by ARDS and hypotension. (Table 8)

**Table 8. Multivariate Logistic Regression Analysis**

| Variable                  | Adjusted OR | 95% CI     | p value |
|---------------------------|-------------|------------|---------|
| Altered sensorium         | 4.82        | 1.18–19.68 | 0.028   |
| Hypotension               | 5.76        | 1.32–25.07 | 0.020   |
| Acute kidney injury       | 4.29        | 1.09–16.86 | 0.037   |
| ARDS                      | 7.98        | 1.77–35.97 | 0.007   |
| MODS                      | 9.86        | 2.08–46.74 | 0.004   |
| Serum creatinine >2 mg/dL | 3.62        | 1.01–13.02 | 0.048   |

Receiver operating characteristic analysis demonstrated excellent predictive performance for serum creatinine (AUC=0.891), followed by CRP (AUC=0.846), serum albumin (AUC=0.843), platelet count (AUC=0.832), and serum bilirubin (AUC=0.809). All evaluated biomarkers showed statistically significant discriminatory ability for predicting mortality (p<0.001), with serum creatinine providing the highest diagnostic accuracy. (Table 9)

**Table 9. ROC Curve Analysis for Prediction of Mortality**

| Parameter        | Cut-off                 | AUC   | 95% CI      | Sensitivity (%) | Specificity (%) | p value |
|------------------|-------------------------|-------|-------------|-----------------|-----------------|---------|
| Platelet count   | 84 ×10 <sup>3</sup> /μL | 0.832 | 0.732–0.931 | 85.7            | 73.7            | <0.001  |
| Serum creatinine | 2.1 mg/dL               | 0.891 | 0.816–0.967 | 85.7            | 81.6            | <0.001  |
| Serum bilirubin  | 3.0 mg/dL               | 0.809 | 0.692–0.925 | 78.6            | 75.0            | <0.001  |
| Serum albumin    | 2.6 g/dL                | 0.843 | 0.743–0.942 | 78.6            | 82.9            | <0.001  |
| CRP              | 112 mg/L                | 0.846 | 0.747–0.945 | 85.7            | 76.3            | <0.001  |

## DISCUSSION

Scrub typhus continues to be an important cause of acute undifferentiated febrile illness in tropical countries, with the potential to progress rapidly to life-threatening multisystem disease if diagnosis and treatment are delayed. In the present study, the in-hospital mortality was 15.6%, which is comparable to the mortality reported by Chrispal et al. and slightly higher than that reported by Bhargava A et al., likely reflecting differences in referral patterns and disease severity among tertiary care centers [11,12]. Similar to previous reports, fever was the predominant presenting symptom, while headache, myalgia, and gastrointestinal symptoms were frequently encountered. Eschar was identified in only 30.0% of patients, reinforcing that its absence should not exclude the diagnosis, as previous studies have reported eschar frequencies ranging from 17% to 46% [11,12]. These findings further emphasize why scrub typhus is often referred to as the "great mimicker." The present study demonstrated frequent multisystem involvement, with hepatitis (46.7%), thrombocytopenia (43.3%), and acute kidney injury (26.7%) being the most common complications. Respiratory complications including ARDS occurred

in 17.8% of patients, while 21.1% required ICU admission and 16.7% required mechanical ventilation. Similar patterns of organ dysfunction have been described by Griffith et al., who observed that respiratory failure, renal dysfunction, and circulatory shock were the predominant manifestations among critically ill patients with scrub typhus requiring intensive care [13]. Likewise, Gaba S et al. reported hepatic dysfunction, acute kidney injury, and respiratory distress as the commonest organ dysfunctions associated with severe disease [14]. The underlying endothelial injury and widespread vasculitis caused by *Orientia tsutsugamushi* explain the extensive multiorgan involvement observed in severe infection.

Comparison between survivors and non-survivors in the present study demonstrated that older age, diabetes mellitus, hypertension, altered sensorium, hypotension, thrombocytopenia, elevated serum creatinine, hyperbilirubinemia, elevated AST, hypoalbuminemia, and elevated CRP were significantly associated with mortality. Furthermore, patients who developed ARDS, acute kidney injury, septic shock, or MODS had substantially higher mortality. These observations are consistent with those of Chrispal et al., who identified ARDS, altered sensorium, shock, and metabolic acidosis as independent predictors of death [11]. Similarly, Bhargava et al. demonstrated that ARDS and acute kidney injury were the strongest predictors of mortality in patients with scrub typhus, while Lee et al. reported that absence of eschar, ICU admission, and higher severity scores independently predicted fatal outcomes [12,15]. Together, these findings suggest that early recognition of neurological impairment, circulatory instability, respiratory failure, and renal dysfunction is essential for improving survival.

Multivariate logistic regression in the present study identified altered sensorium, hypotension, acute kidney injury, ARDS, MODS, and elevated serum creatinine as independent predictors of mortality, while ROC analysis demonstrated excellent predictive performance of serum creatinine, CRP, serum albumin, platelet count, and serum bilirubin. These findings support the concept that simple clinical assessment combined with routinely available laboratory investigations can effectively identify high-risk patients at admission. Early initiation of doxycycline, aggressive hemodynamic resuscitation, close monitoring for organ dysfunction, and timely ICU referral in patients exhibiting these predictors may substantially reduce mortality. Therefore, prompt recognition of severe disease and early risk stratification remain fundamental strategies for improving outcomes in scrub typhus.

## CONCLUSION

Scrub typhus remains a significant cause of acute febrile illness with the potential to rapidly progress to severe multisystem involvement and death if not recognized and treated promptly. The present study identified altered sensorium, hypotension, acute kidney injury, acute respiratory distress syndrome, multiple organ dysfunction syndrome, and elevated serum creatinine as independent predictors of in-hospital mortality. Additionally, routine laboratory parameters such as platelet count, serum bilirubin, serum albumin, and C-reactive protein demonstrated good predictive utility for adverse outcomes. Early recognition of these high-risk clinical and laboratory indicators, prompt initiation of appropriate antimicrobial therapy, vigilant monitoring, and timely intensive care intervention are essential to improve survival and reduce mortality among patients with scrub typhus.

**Acknowledgement:** None

**Funding:** None

**Conflict of Interest:** None.

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