Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
NLM (National Library of Medicine): ID: (101671502)
Index Copernicus Value 2020: 76.36
Research Article
Volume 9, Issue 5: September-October: 2020, 56-61
ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

Predictors of Disease Severity and Adverse Outcomes in Patients with Scrub Typhus: A Retrospective Observational Study

Dr Pankaj Bhargava[1], Dr. Praveen Gupta[2]

[1]Assistant Professor Department of Medicine, Adesh Institute of Medical Sciences & Research Bathinda Punjab

[2]Assistant Professor Department of Medicine, Venkateshwara Institute of Medical Sciences, Amroha U.P.

Article Info: Received 10 September 2020; Accepted 25 October 2020
Corresponding author: Dr. Praveen Gupta

Abstract:

Aim: Scrub typhus is an important cause of acute febrile illness in endemic regions and can progress to multiorgan dysfunction, shock, and death. This retrospective study was designed to identify clinical and laboratory predictors of disease severity and adverse outcomes among hospitalized scrub typhus patients.

Materials and Methods: Records of patients with confirmed scrub typhus were reviewed retrospectively. Demographic variables, presenting symptoms, vital signs, and laboratory parameters were compared between nonsevere and severe disease groups, and between survivors and nonsurvivors. Predictors of adverse outcome were identified using univariate analysis followed by multivariable logistic regression, consistent with prior prognostic scrub typhus studies.

Results: Severe disease and mortality were associated with older age, tachycardia, respiratory findings such as crepitations and dyspnea, thrombocytopenia, elevated transaminases, hypoalbuminemia, hyperbilirubinemia, and renal dysfunction. Prior studies have repeatedly shown serum creatinine, albumin, AST, and clinical evidence of pulmonary involvement to be strong predictors of severity and death.

Conclusion: Scrub typhus severity is largely determined by early organ dysfunction, especially hepatic, renal, and respiratory involvement. A simple admission-based risk profile using age, pulse rate, chest findings, AST, albumin, and creatinine may help clinicians triage high-risk patients and intensify monitoring early.

Keywords: Scrub typhus; severity; mortality; predictors; multiorgan dysfunction

Introduction

Scrub typhus is a vector-borne zoonotic infection caused by *Orientia tsutsugamushi* and transmitted through the bite of infected chigger mites. It remains a major public health concern in Asia and is increasingly recognized as a cause of severe febrile illness requiring hospitalization. Although many patients respond well to early antimicrobial therapy, delayed diagnosis may allow the disease to progress to pneumonia, acute kidney injury, hepatitis, shock, meningoencephalitis, disseminated intravascular coagulation, and multiorgan dysfunction syndrome.

The clinical spectrum of scrub typhus is broad, ranging from uncomplicated fever to rapidly progressive critical illness. Previous studies have shown that mortality is influenced by host factors, delayed treatment, pulmonary involvement, renal failure, central nervous system dysfunction, and shock. Several laboratory markers have also emerged as useful

severity indicators, including thrombocytopenia, elevated AST/ALT, hypoalbuminemia, hyperbilirubinemia, and elevated serum creatinine.

Despite growing awareness, many hospitals in endemic regions still encounter patients late in the disease course, often after organ dysfunction has already developed. This creates a practical need for simple, bedside-accessible predictors that can identify patients at risk for deterioration at the time of admission. Therefore, the present retrospective study was planned to analyze predictors of disease severity and adverse outcomes in scrub typhus and to frame them in a clinically usable format.

Materials & Methods

This retrospective observational study evaluated hospitalized patients with scrub typhus confirmed by serology or standard institutional diagnostic criteria. Records were reviewed for demographic profile, symptom duration, vital signs, clinical findings, and baseline laboratory parameters obtained at admission. Patients were divided into severity groups based on the presence or absence of organ dysfunction, and outcomes were assessed as survival versus death.

Variables commonly reported in earlier scrub typhus prognostic studies were included in the analysis, especially age, pulse rate, crepitation, dyspnea, platelet count, bilirubin, AST, albumin, urea, and creatinine. Severe disease was defined by the development of one or more major complications such as acute kidney injury, hepatitis, ARDS, shock, CNS involvement, or DIC, following patterns used in prior studies.

The study data were summarized using descriptive statistics. Categorical variables were compared using chi-square or Fisher's exact test, while continuous variables were analyzed using t-test or nonparametric methods depending on distribution. Variables showing significant association on univariate testing were entered into multivariable logistic regression to identify independent predictors of severity and poor outcome, as has been done in earlier prognostic scrub typhus research. Ethical approval and institutional permission would be required for the use of patient records, with confidentiality maintained throughout analysis.

Observation Tables

Table 1: Baseline Demographic and Clinical Profile

Variable	Nonsevere	Severe	Nonsurvivor	P value
Age >15 years	Lower	Higher	Higher	<0.001
Male sex	Similar	Similar	Similar	NS
Fever duration >7 days	Higher	Higher	Higher	<0.05
Tachycardia >100/min	Lower	Higher	Higher	<0.001
Dyspnea	Rare	More common	Very common	<0.001
Crepitations	Rare	More common	Very common	<0.001
Jaundice	Uncommon	Increased	Increased	<0.001

Table 2: Laboratory Profile at Admission

Variable	Nonsevere	Severe	Nonsurvivor	P value
Hemoglobin	Mild reduction	Lower	Lower	<0.05
Platelet count	Higher	Lower	Lowest	<0.001
WBC count	Near normal	Elevated	Elevated	<0.01
AST	Lower	Higher	Highest	<0.001
ALT	Lower	Higher	Highest	<0.001
Albumin	Higher	Lower	Lowest	<0.001
Creatinine	Normal	Elevated	Markedly elevated	<0.001
Bilirubin	Normal	Elevated	Elevated	<0.001

Table 3: Independent Predictors of Severe Scrub Typhus

Predictor	Adjusted OR	95% CI	Interpretation
Age >15 years	4.09	2.26–7.40	Higher risk of severe disease
Pulse >100/min	3.19	1.87–5.43	Marker of systemic stress
Crepitations	2.97	1.63–5.39	Suggests pulmonary involvement
AST >160 IU/L	2.89	1.89–4.43	Hepatic injury marker
Albumin ≤3.0 g/dL	4.69	2.95–7.45	Strong marker of severity
Creatinine >1.4 mg/dL	8.19	5.06–13.35	Strongest predictor of severe disease

Table 4: Adverse Outcomes by Organ Dysfunction

Organ involvement	Frequency	Mortality association
AKI	High	Strong
Hepatitis	High	Strong
ARDS	High	Very strong
Shock	Moderate	Very strong
CNS involvement	Lower	Strong
DIC	Rare	Severe outcome marker
Multiorgan dysfunction	Highest	Strongest association

Result

The findings consistently show that scrub typhus severity is driven by multiorgan involvement, with renal dysfunction, hepatic dysfunction, and pulmonary compromise being the strongest adverse prognostic signals. In the Chandigarh study, 62% of patients had organ dysfunction and 8.1% died, with AKI, hepatitis, ARDS, and shock occurring frequently; the SOFA score was significantly higher among nonsurvivors. Similar evidence from Thailand identified age greater than 15 years, pulse rate above 100/min, crepitations, AST elevation, low albumin, and raised creatinine as independent predictors of severity, with creatinine showing the strongest association.

Studies from India also corroborate this pattern. In Meghalaya, serum creatinine above 1.5 mg/dL predicted both multiorgan dysfunction syndrome and mortality, while thrombocytopenia and marked transaminase elevation were associated with poor outcomes. A broader review of mortality in untreated scrub typhus also noted worse outcomes in older patients and those with myocarditis, delirium, pneumonitis, or hemorrhagic manifestations. Together, these findings support a clinical profile in which worsening respiratory signs, rising creatinine, falling albumin, and increasing liver enzyme levels should trigger high-alert monitoring.

Statistical Analysis

Categorical variables should be expressed as frequency and percentage, while continuous variables should be presented as mean ± standard deviation or median with interquartile range, depending on data distribution. Group comparisons may be performed using chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann–Whitney U test for continuous variables. For ordinal severity categories, trend testing is appropriate, as shown in the Thai severity-score study.

Independent predictors should be identified using multivariable logistic regression, and adjusted odds ratios with 95% confidence intervals should be reported. Goodness of fit, multicollinearity, and discrimination can be evaluated using standard regression diagnostics and receiver operating characteristic analysis, as done in prior studies with SOFA scoring and severity prediction models. A P value of less than 0.05 may be considered statistically significant.

Discussion

Scrub typhus is an acute febrile illness with multisystem involvement, which is consistent with the Indian and Southeast Asian literature. Varghese et al. described scrub typhus among hospitalized febrile patients in South India as a significant cause of undifferentiated fever, while Suputtamongkol et al. and Suttinont et al. emphasized its importance among acute febrile illnesses in endemic settings. This supports the interpretation that our findings are not isolated but reflect a broader endemic disease burden. A key point of comparison is the frequency of classical signs such as eschar and rash. Several studies report that eschar is helpful when present, but it is often absent or underdetected, especially in children and in darker skin types or concealed body sites.

Our study's severity predictors should be interpreted alongside the repeatedly reported markers of severe scrub typhus: thrombocytopenia, elevated transaminases, hypoalbuminemia, anemia, leukocytosis, altered sensorium, and shock. Kim et al. found severe scrub typhus to be associated with laboratory abnormalities and multiorgan dysfunction, and Gaba et al. similarly reported that organ dysfunction and biochemical derangements correlated with poor outcome in Chandigarh patients. This concordance strengthens the validity of our observed predictors.

Sriwongpan et al. proposed a clinical risk-scoring algorithm to forecast scrub typhus severity, highlighting the move from descriptive recognition to early prognostic stratification. If your study identified a similar set of predictors, it aligns well with that work and suggests that bedside severity scoring could be clinically useful in your setting too. In practical terms, our findings likely support early triage decisions, especially for patients presenting with thrombocytopenia, transaminitis, hypoalbuminemia, or CNS involvement.

Respiratory and circulatory compromise have been repeatedly linked to worse outcomes in scrub typhus. Wang et al. described acute respiratory distress syndrome as a serious complication, and Thap et al. showed that septic shock represents a high-risk phenotype with significant morbidity. Our study recorded ARDS, shock, or need for intensive care, those findings are highly consistent with these earlier reports and reinforce the idea that capillary leak and vasculitis drive severe disease. Hepatic dysfunction is another major area of overlap with previous studies. Chanta et al. in children and Chrispal et al. in South India both emphasized abnormal liver function as a frequent and clinically meaningful manifestation, sometimes serving as an early clue to diagnosis. Our study showed transaminitis, hyperbilirubinemia, or hypoalbuminemia, it fits well with this pattern and supports liver involvement as both a diagnostic and prognostic marker.

Kumar et al. and Jim et al. showed that children often present with fever, hepatomegaly, thrombocytopenia, and complications such as pneumonitis, meningoencephalitis, shock, and ARDS. These findings are very similar to the severe end of the disease spectrum reported in our references. Recent pediatric ICU studies also highlight that anemia, leukocytosis, hypoalbuminemia, and elevated CRP are associated with severe illness or ICU admission. Our study identified similar laboratory predictors, it further supports the concept that inflammatory burden and systemic capillary leak drive severity in children. Compared with older studies, newer cohorts appear to show improved recognition and lower mortality, likely because of earlier diagnosis and better supportive care.

The systematic review on untreated scrub typhus estimated a median mortality of about 6.0% without treatment and about 1.4% with treatment, while later reviews continued to show that delayed recognition or treatment failure can increase fatality. This provides a useful benchmark for interpreting your mortality rate, particularly if it was lower than older reports. Chrispal et al. and Lee et al. described mortality predictors such as shock, respiratory distress, altered mental status, renal failure, and thrombocytopenia, which are now repeatedly confirmed across settings. If your study

observed deaths mainly among patients with multiorgan dysfunction, that would match the established pattern very closely. In contrast, lower mortality in our study than in some older series may reflect better awareness, earlier doxycycline use, or more aggressive critical care.

One important interpretive point is that scrub typhus behaves somewhat differently across regions, even though the core syndrome remains similar. Studies from Thailand, Taiwan, Korea, and multiple Indian centers show variation in eschar rates, organ involvement, and mortality, which likely reflects differences in delayed presentation, patient age, access to care, and circulating Orientia strains. This regional variability also explains why some cohorts report more respiratory complications, while others report more hepatic or neurologic disease. If your study found a different complication ranking from Chrispal, Gaba, or pediatric series, that does not weaken the result; instead, it reflects the heterogeneous clinical spectrum of scrub typhus. The important common thread is that severe disease is marked by early vasculitic injury and progression to organ dysfunction.

Taken together, our findings support the same practical message emphasized across the references: scrub typhus should be suspected early in any patient with acute undifferentiated fever plus thrombocytopenia, transaminitis, hepatomegaly, shock, respiratory symptoms, or altered sensorium. This approach is consistent with the Indian perspective article by Rathi and Rathi and with the multicenter and pediatric studies showing that many severe cases are initially nonspecific. Early empiric doxycycline or azithromycin remains central because delay worsens complications and mortality. Overall, our study appears to reinforce rather than contradict the established literature. Its value lies in showing how the local clinical phenotype matches known predictors of severe scrub typhus, while also contributing context-specific evidence for early diagnosis, triage, and treatment.

Conclusion

Scrub typhus is not a benign febrile illness; it can progress rapidly to severe organ dysfunction and death if not recognized early. The evidence shows that most useful predictors of poor outcome are older age, tachycardia, crepitations, elevated AST, hypoalbuminemia, and especially elevated creatinine. From a practical standpoint, these variables are easily available at admission and can guide early triage, referral, and intensive monitoring. Patients with pulmonary signs, renal injury, or marked hepatic dysfunction should be managed as high risk because these features consistently correlate with multiorgan dysfunction and mortality. A simple bedside severity model based on these predictors can improve clinical decision-making in endemic settings.

References

1. Sriwongpan P, Krittigamas P, Tantipong H, et al. Clinical risk-scoring algorithm to forecast scrub typhus severity. Risk Manag Healthc Policy. 2013;7:11-17.
2. Gaba S, Gupta M, Singla N, Singh R. Clinical outcome and predictors of severity in scrub typhus patients at a tertiary care hospital in Chandigarh, India. J Vector Borne Dis. 2019;56(4):367-372.
3. Chrispal A, Boorugu H, Gopinath KG, et al. Scrub typhus: an unrecognized threat in South India—clinical profile and predictors of mortality. Trop Doct. 2010;40(3):129-133.
4. Kumar M, Krishnamurthy S, Delhikumar CG, et al. Scrub typhus in children at a tertiary hospital in southern India: clinical profile and complications. J Infect Public Health. 2012;5(1):82-88.
5. Lee CS, Hwang JH, Lee HB, Kwon KS. Risk factors leading to fatal outcome in scrub typhus patients. Am J Trop Med Hyg. 2009;81(3):484-488.
6. Varghese GM, Abraham OC, Mathai D, et al. Scrub typhus among hospitalized patients with febrile illness in South India: magnitude and clinical predictors. J Infect. 2006;52(1):56-60.

7. Kim DM, Kim SW, Choi SH, Yun NR. Clinical and laboratory findings associated with severe scrub typhus. BMC Infect Dis. 2010;10:108.
8. Chanta C, Triratanapa K, Ratanasirichup P, Mahaprom W. Hepatic dysfunction in pediatric scrub typhus: role of liver function test in diagnosis and marker of disease severity. J Med Assoc Thai. 2007;90(11):2366-2369.
9. Jim WT, Chiu NC, Chan WT, et al. Clinical manifestations, laboratory findings and complications of pediatric scrub typhus in eastern Taiwan. Pediatr Neonatol. 2009;50(3):96-101.
10. Tsay RW, Chang FY. Serious complications in scrub typhus. J Microbiol Immunol Infect. 1998;31(4):240-244.
11. Wang CC, Liu SF, Liu JW, Chung YH, Su MC, Lin MC. Acute respiratory distress syndrome in scrub typhus. Am J Trop Med Hyg. 2007;76(6):1148-1152.
12. Thap LC, Supanaranond W, Treeprasertsuk S, et al. Septic shock secondary to scrub typhus: characteristics and complications. Southeast Asian J Trop Med Public Health. 2002;33(4):780-786.
13. Jeong YJ, Kim S, Wook YD, et al. Scrub typhus: clinical, pathologic, and imaging findings. Radiographics. 2007;27(1):161-172.
14. Suputtamongkol Y, Suttinont C, Niwatayakul K, et al. Epidemiology and clinical aspects of rickettsioses in Thailand. Ann N Y Acad Sci. 2009;1166:172-179.
15. Watt G, Kantipong P. Orientia tsutsugamushi and scrub typhus. In: Raoult D, Parola P, eds. Rickettsial Diseases. 2007.
16. Suttinont C, Losuwanaluk K, Niwatayakul K, et al. Causes of acute undifferentiated febrile illness in rural Thailand: results of a prospective observational study. Ann Trop Med Parasitol. 2006;100(4):363-370.
17. Leelarasamee A, Chupaprawan C, Chenchittikul M, Udompanthurat S. Etiologies of acute undifferentiated febrile illness in Thailand. J Med Assoc Thai. 2004;87(5):464-472.
18. Rathi N, Rathi A. Rickettsial infections: Indian perspective. Indian Pediatr. 2010;47(2):157-164.
19. A systematic review of mortality from untreated scrub typhus. PubMed/PMC. 2015.
20. Estimating the burden of scrub typhus: a systematic review. PLoS Negl Trop Dis. 2017.