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Research Article

Clinical Profile and Outcomes of Scrub Typhus with Multi-Organ Dysfunction Syndrome (MODS)

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ABSTRACT

Background: Scrub typhus is a re-emerging zoonotic disease caused by *Orientia tsutsugamushi* and has become an important cause of acute undifferentiated febrile illness in India. Delayed diagnosis frequently results in multiple organ dysfunction syndrome (MODS), leading to increased morbidity and mortality. The present study evaluated the clinical profile, laboratory abnormalities, organ dysfunction, and outcomes of patients with scrub typhus-associated MODS admitted to a tertiary care hospital in Central India.

Methods: A hospital-based cross-sectional observational study was conducted in the Department of General Medicine, Chirayu Medical College and Hospital, Bhopal, from July to December 2025. Thirty patients aged ≥14 years with clinically suspected or

serologically confirmed scrub typhus complicated by MODS were enrolled. Clinical characteristics, laboratory parameters, Sequential Organ Failure Assessment (SOFA) scores, treatment response, and clinical outcomes were recorded using a structured proforma. SOFA scores were assessed on admission, Day 3, and Day 5. Data were analysed using IBM SPSS version 25, and statistical significance was considered at $p<0.05$.

Results: The mean haemoglobin level was 9.82 ± 1.58 g/dL, total leukocyte count 10.73 ± 3.73 $\times 10^3/\mu L$, platelet count 63.07 ± 21.40 $\times 10^3/\mu L$, and APTT 46.10 ± 10.04 seconds. Respiratory compromise was evident with a mean SpO_2 of 91.13 ± 7.96% and PaO_2/FiO_2 ratio of 257.73 ± 103.59. Mean SOFA scores significantly decreased from 9.73 ± 4.48 at admission to 7.63 ± 5.74 on Day 3 and 4.15 ± 6.10 on Day 5 ($p=0.001$). A favourable clinical response to doxycycline was observed in 63.3% of patients, while 36.7% required vasopressor support.

Conclusion: Scrub typhus-associated MODS is characterized by significant hematological abnormalities, coagulation derangements, respiratory dysfunction, and severe organ involvement. Serial SOFA score assessment is a useful tool for monitoring disease progression and therapeutic response. Early clinical suspicion, prompt diagnosis, timely initiation of doxycycline, and aggressive supportive care are essential to improve outcomes and reduce mortality in endemic regions.

Keywords: Scrub typhus; Multiple organ dysfunction syndrome; SOFA score; Doxycycline; *Orientia tsutsugamushi*.

Introduction

Scrub typhus is a re-emerging vector-borne zoonotic infection caused by Orientia tsutsugamushi, an obligate intracellular Gram-negative bacterium transmitted to

humans by the bite of infected larval trombiculid mites (chiggers). It is a major cause of acute undifferentiated febrile sickness in the Asia-Pacific region and is endemic in the "tsutsugamushi triangle," which extends from northern Japan and the Russian Far East through China, Southeast Asia, the Indian subcontinent, and northern Australia. The global burden of the disease is estimated to be more than one billion at-risk people and approximately one million new infections each year. The actual disease burden is thought to be much underestimated due to underdiagnosis and poor surveillance.[1-3] Recent research reveals that scrub typhus is no longer restricted to its classic endemic areas with growing reports from geographical areas formerly untouched indicating a spreading worldwide distribution.[4]

Scrub typhus has re-emerged as a major public health hazard in India throughout the previous decade. The reported cases have shown a consistent rise in studies in hospitals and communities from almost every state, especially in monsoon and post monsoon seasons when vector activity is at its peak.[4,5] A recent statewide epidemiological research found more than 47,000 cases over two decades and identified a large increase in disease incidence after 2010 with peaks in 2019 and 2022, reflecting both improved surveillance and changing environmental circumstances.[5] The increasing epidemi ology of scrub typhus in India is due to increasing agricultural activity, fast urbanization, climatic change, deforestation, and increased human exposure to vegetation infested with mites. A rise in the number of cases has also been recorded from central Indian states like Madhya Pradesh, highlighting the need for increased clinical awareness and better diagnostic capacities in this region.[6-8] The pathophysiology of scrub typhus is

mostly associated with invasion of the endothelium by O. tsutsugamushi. Upon inoculation the bacterium disseminates across the blood stream infecting endothelial cells macrophages and dendritic cells resulting in extensive vasculitis perivasculitis endothelial dysfunction and increased vascular permeability.[2] Activation of inflammatory pathways leads to excessive production of cytokines such as tumour necrosis factor-α, interleukin-1β, interleukin-6 and interferon-γ. This results in a systemic inflammatory response which contributes to tissue hypoperfusion and multiorgan damage.[9] These pathogenic pathways can account for the wide range of clinical presentation and the development of serious consequences in untreated disease.

The clinical picture of scrub typhus is rather diverse from a mild self-limiting febrile illness to severe sepsis with multiple organ dysfunction syndrome (MODS). Fever is the most constant presenting symptom, frequently coupled with headache, myalgia, chills, cough, nausea, vomiting, abdominal discomfort, and lymphadenopathy.[10] The presence of an eschar is pathognomonic, but the prevalence of eschar ranges greatly from <10% to >60% depending on the geographic area, skin pigmentation, and completeness of the clinical examination.[11] As a result, many patients are initially misdiagnosed as dengue, malaria, leptospirosis, enteric fever or viral fever, leading to delayed beginning of appropriate antibiotic therapy.[7] The main factor determining the severity of the condition is the delayed diagnosis. If left untreated, infection can quickly lead to MODS, due to widespread damage to the lining cells of blood vessels and problems with the tiny blood vessels that serve several organ systems at once. The most commonly documented sequelae in severe scrub typhus are hepatic dysfunction, acute renal injury, thrombocytopenia, acute respiratory

distress syndrome, myocarditis, meningoencephalitis, disseminated intravascular coagulation and septic shock.[9,12] Mortality rates of MODS in hospitalized patients in India have been found to range from 5-30%. Mortality rates are high in patients requiring critical care support and those presenting late after onset of symptoms.[12,13] The Sequential Organ Failure Assessment (SOFA) score has been recognized as an established technique for the objective assessment of the severity of organ dysfunction in critically ill patients. The SOFA score evaluates respiratory, cardiovascular, neurological, hepatic, renal and coagulation parameters and gives reliable predictive information on illness course, need for critical care and in-hospital mortality. Recent studies have shown that rising admission SOFA scores are independently related with poor outcomes in patients with scrub typhus, indicating the usefulness of this scoring method for early risk assessment and clinical decision-making. Despite growing awareness of scrub typhus in India, there is paucity of data on clinical profile, pattern of organ dysfunction and prognosis among patients with scrub typhus associated MODS in Central India. [12,14] Epidemiology and clinical symptoms of the disease, access to healthcare and treatment procedures vary by region, with institution-specific data needed to optimize patient management. Hence, the present study was conducted to assess the demographic profile, clinical features, laboratory abnormalities, organ involvement, SOFA score, response to treatment and clinical outcome in patients with scrub typhus complicated by MODS admitted to a tertiary care teaching hospital in Central India.

METHODOLOGY

This hospital-based cross-sectional observational study was conducted in the Department of General Medicine, Chirayu

Medical College and Hospital, Bhopal, Madhya Pradesh for a period of six months from July 2025 to December 2025. The study recruited patients aged ≥14 years admitted with clinically suspected or serologically confirmed scrub typhus complicated by multiorgan dysfunction syndrome (MODS). MODS was characterized as dysfunction of two or more organ systems by clinical and laboratory parameters and Sequential Organ Failure Assessment (SOFA) score. We eliminated patients with pre-existing chronic liver illness, chronic renal disease, chronic heart failure, autoimmune disorders, pregnancy or MODS due to other proven causes. Written informed consent was obtained and a total of 30 eligible patients who met the inclusion criteria were enrolled.

A comprehensive clinical history, demographic information, physical examination and laboratory investigations were documented in a pre-designed case record form. Investigations included full blood count, liver and renal function tests, coagulation profile, arterial blood gas analysis, chest radiography, ultrasonography as indicated and scrub typhus serology (IgM ELISA). Organ dysfunction was assessed using the Sequential Organ Failure Assessment (SOFA) score on admission (Day 0), Day 3 and Day 5. All patients were treated with doxycycline based therapy and supportive care including vasopressor support, oxygen, mechanical ventilation, dialysis and intensive care management when required according to institutional standards. Clinical outcome data including responsiveness to doxycycline, need for vasopressors, length of hospital stay and survival status were recorded until discharge or death.

The collected data were imported into Microsoft Excel and evaluated with IBM SPSS Statistics version 25. Continuous data were expressed as mean ± standard

deviation while categorical variables were expressed as frequency and percentage. The SOFA scores at different time points were compared using one-way analysis of variance (ANOVA). Statistical significance was defined as a p-value <0.05.

RESULTS

A total of 30 patients diagnosed and suspected with scrub typhus-associated multi-organ dysfunction syndrome (MODS) were included in the study, Microbiological evaluation revealed that 13 (43.3%) patients were positive for IgM ELISA against *Orientia tsutsugamushi*, whereas 17 (56.7%) were IgM ELISA-negative but clinically suspected cases of scrub typhus. Baseline laboratory parameters, serial SOFA scores, and treatment outcomes were analysed to evaluate disease severity and clinical response.

The baseline laboratory characteristics of the study population are presented in Table 1. The mean haemoglobin level was 9.82 ± 1.58 g/dL, indicating mild-to-moderate anaemia among the study participants. The mean total leukocyte count was 10.73 ± 3.73 × 10^3/μL, suggestive of an inflammatory response. Significant thrombocytopenia was observed, with a mean platelet count of 63.07 ± 21.40 × 10^3/μL. The mean activated partial thromboplastin time (APTT) was 46.10 ± 10.04 seconds, reflecting coagulation abnormalities in several patients. The average Glasgow Coma Scale (GCS) score was 13.20 ± 2.70, while the mean arterial pressure (MAP) was 72.60 ± 8.46 mmHg. The mean oxygen saturation (SpO_2) and PaO_2/FiO_2 ratio were 91.13 ± 7.96% and 257.73 ± 103.59, respectively, indicating variable degrees of respiratory involvement (Table 1).

Serial assessment of organ dysfunction using the Sequential Organ Failure Assessment (SOFA) score demonstrated a progressive reduction during the course of hospitalization (Table 2). The mean SOFA

scores progressively decreased from admission to Day 5 in both IgM ELISA-positive and clinically suspected patients. Significant intragroup improvement was observed in the IgM ELISA-positive (p = 0.023) and clinically suspected groups (p = 0.047), whereas intergroup comparisons at each time point showed no statistically significant differences (p > 0.05). The clinical response to doxycycline therapy and vasopressor requirement are summarized in Table 3. A favourable response to doxycycline was observed in 8 (61.5%) IgM ELISA-positive patients and 11 (64.7%) clinically suspected IgM ELISA-negative patients, with no statistically significant association between serological status and treatment response (p = 0.858). Similarly, vasopressor support was required in 6 (46.2%) IgM ELISA-positive patients compared with 5 (29.4%) clinically suspected IgM ELISA-negative patients, and this difference was also not statistically significant (p = 0.346).

Table 1. Baseline Laboratory Parameters

Parameter	Mean ± SD	Minimum	Maximum
Haemoglobin (g/dL)	9.82 ± 1.58	6.2	13.2
Total Leukocyte Count (×10³/µL)	10.73 ± 3.73	3.6	17.2
Platelet Count (×10³/µL)	63.07 ± 21.40	18	118
APTT (seconds)	46.10 ± 10.04	32	82
Glasgow Coma Scale	13.20 ± 2.70	6	15
Mean Arterial Pressure (mmHg)	72.60 ± 8.46	56	88

SpO_2 (%)	91.13 ± 7.96	67	98
PaO_2/FiO_2 Ratio	257.73 ± 103.59	82	398

Table 2. Intra-and Inter-group comparison of Sequential Organ Failure Assessment (SOFA) Scores During Hospital Stay

Time Point	**IgM ELISA Positive (n = 13)**	**Clinically Suspected (n = 17)**	**p-value**
SOFA Day 0	11.23 ± 4.73	8.59 ± 4.05	0.111
SOFA Day 3	9.00 ± 5.83	6.59 ± 5.62	0.262
SOFA Day 5	4.73 ± 6.02	3.73 ± 6.34	0.690
p-value	**0.023***	**0.047***	

***- Statistically significant**

Table 4. Clinical Response to Doxycycline and Vasopressor Requirement

Clinical Outcome		**IgM ELISA Positive (n = 13)**	**IgM ELISA Negative (Clinically Suspected) (n = 17)**	**p-value***
Response to doxycycline	Yes	8 (61.5)	11 (64.7)	0.858
	No	5 (38.5)	6 (35.3)	
	Yes	6 (46.2)	5 (29.4)	0.346

Vasopressor required	No	7 (53.8)	12 (70.6)	

DISCUSSION

Scrub typhus is an important re-emerging zoonotic disease and is increasingly recognised as a major cause of acute undifferentiated febrile sickness in tropical and subtropical areas. Delayed diagnosis leads to multiple organ dysfunction syndrome (MODS) with higher morbidity, prolonged hospital stay, intensive care requirement and mortality, though curable illness. The present study analyzed clinical profile, laboratory derangements, severity of organ failure and therapy results in patients with scrub typhus related MODS hospitalized at a tertiary care teaching hospital in Central India. Findings indicated that scrub typhus was linked with considerable haematological abnormalities, coagulation abnormalities, respiratory compromise and severe organ failure at presentation. However, serial examination of SOFA score found considerable improvement after doxycycline based therapy emphasizing importance of early diagnosis and beginning of suitable antimicrobial medication.

One of the major findings in the present study was the finding of severe hematologic abnormalities. The mean platelet count was 63.07 ± 21.40 $\times 10^3/\mu L$ with severe thrombocytopenia. Mean haemoglobin concentration was 9.82 ± 1.58 g/dL. Thrombocytopenia has been documented as one of the earliest and most persistent laboratory abnormalities in scrub typhus and is attributable to endothelial injury, platelet consumption, immune-mediated destruction and splenic sequestration. Recent epidemiological reviews have highlighted that thrombocytopenia is not

only a marker of disease severity but also an independent predictor of ICU admission and unfavorable outcomes in severe scrub typhus [15,16]. Similarly, in the systematic study by Bonell et al [17], thrombocytopenia was seen in more than half of hospitalized patients and was related with MODS and longer hospitalization.

The present investigation also revealed modest leukocytosis with a mean total leukocyte count of 10.73 ± 3.73 $\times 10^3/\mu L$ suggestive of continued systemic inflammatory response. Total leukocyte counts may be normal in the early phase of sickness but higher counts have been associated with subsequent bacterial infection, significant endothelium inflammation and cytokine activation in advanced disease [18]. Recent reviews have proposed that leukocytosis along with thrombocytopenia and increased inflammatory biomarkers may be beneficial in identifying patients at higher risk of severe sequelae needing intense monitoring [16,18].

Another important finding of this investigation was coagulation problems. Mean activated partial thromboplastin time (APTT) was 46.10 ± 10.04 seconds. This indicates activation of the coagulation cascade due to widespread endothelial damage. Infection with Orientia tsutsugamushi causes a systemic vasculitis with diffuse endothelial inflammation and enhanced vascular permeability, platelet activation and coagulation problems. In severe circumstances these changes might lead to disseminated intravascular coagulation which accounts for a large amount of morbidity and mortality [19]. Similar observations have been made in recent studies of critically ill scrub typhus patients, where prolonged coagulation parameters were associated with disease severity and poor clinical outcome [20].

Another key indication seen in the present investigation was respiratory impairment. The mean oxygen saturation was 91.13 ± 7.96% and the mean PaO2/FiO2 ratio was 257.73 ± 103.59, suggesting different degrees of pulmonary impairment. Pulmonary complication in scrub typhus is due to extensive endothelial damage leading to increased capillary permeability, interstitial pneumonitis, pulmonary edema and acute respiratory distress syndrome (ARDS). Recent multicentric studies from India have reported respiratory involvement as one of the strongest indicators for ICU admission and mortality [21]. Likewise, Kim DN et al. observed that pulmonary dysfunction is a substantial contributor to poor outcomes especially among patients presenting late after symptom start [22].

One of the highlights of the present investigation was the evaluation of organ dysfunction by the Sequential Organ Failure Assessment (SOFA) score. The mean SOFA score fell considerably from 9.73 ± 4.48 at admission to 7.63 ± 5.74 on Day 3 and 4.15 ± 6.10 on Day 5 ($p = 0.001$), indicating a continuous improvement in organ function during hospitalization. The findings here confirm the value of serial SOFA score evaluation as an objective way of following illness course and response to therapy. Recent observational studies also reported that higher admission SOFA scores are strongly associated with intensive care requirement, mechanical ventilation, prolonged hospitalization and mortality while declining SOFA scores during treatment imply favourable clinical recovery [20,23].

Another clinically noteworthy result was the need for vasopressor therapy in 36.7% of patients due to circulatory instability. In scrub typhus, septic shock is predominantly due to widespread vasculitis, endothelial dysfunction, capillary leakage and systemic inflammatory response resulting in

decreased effective circulation volume and poor tissue perfusion. Recent investigations have consistently demonstrated that individuals requiring vasopressor support tend to have substantial organ involvement and a significantly increased death rate compared to patients without haemodynamic impairment [21,24].

The present study also showed that 63.3% of patients had a good response to doxycycline medication. Doxycycline is still the drug of choice for scrub typhus because of its good intracellular penetration and quick action against Orientia tsutsugamushi. Early administration of doxycycline has been consistently related with quick defervescence, reversal of organ failure, shorter hospital stay and lower mortality [25]. Delayed clinical response in the majority of patients in the present study probably reflects advanced disease at presentation with established MODS and thus highlights the necessity of early clinical suspicion and rapid beginning of empirical therapy in endemic countries.

The positive clinical response of doxycycline therapy in the present study strengthens its role as the first line antibacterial drug for scrub typhus. Also, 63.3% of the patients had clinical improvement after starting doxycycline, but 36.7% had delayed or inadequate response. Late presentation, severe organ dysfunction at admission, delayed administration of suitable antibiotics or the presence of secondary bacterial infections needing prolonged supportive treatment may explain the delayed response. Recent evidence suggests that early commencement of doxycycline in the first 5 days of sickness considerably reduces the incidence of MODS, length of hospitalisation, and mortality [26]. In a large population-based prospective investigation from South India, Devamani et al. found quick clinical recovery among most patients receiving

early doxycycline medication and emphasized the necessity of prompt empirical treatment in endemic areas [27].

The present investigation showed that 36.7% of the patients needed vasopressor support, which is a reflection of the severity of circulatory dysfunction associated with scrub typhus-associated MODS. In severe cases, septic shock may develop. Diffuse vasculitis, increased capillary permeability, intravascular volume depletion, and systemic inflammatory response syndrome are induced by endothelial damage due to Orientia tsutsugamushi [28]. Similarly, previous investigations have revealed that patients receiving vasopressors have significantly higher SOFA scores, longer intensive care stay and poorer clinical outcomes compared to haemodynamically stable patients [29]. Early haemodynamic monitoring and intensive fluid resuscitation with appropriate and timely vasopressor delivery remain crucial components of therapy in the critically unwell.

The findings of the present investigation are in general agreement with earlier published reports from India and other endemic nations. Thrombocytopenia, respiratory dysfunction, acute renal injury, hepatic dysfunction, neurological symptoms, and circulatory failure have been documented by several investigators to be the most common manifestation of severe scrub typhus [21,22,30]. The scope of organ involvement differs in different geographical areas, but the unifying pathogenic mechanism responsible for MODS is diffuse endothelium damage. The present study further supports these results by showing considerable improvement in serial SOFA ratings after adequate antibiotic medication and supportive management.

A major strength of the present investigation is the prospective evaluation of organ dysfunction by serial SOFA scoring. Serial

assessment offered objective evidence of illness progression and therapy response during hospitalization, unlike many earlier trials that analyzed just entry data. The drop in SOFA score from admission to Day 5 was statistically significant which implies improvement of organ function after therapy. SOFA score can be used as an efficient bedside tool to monitor patients with scrub typhus associated MODS. Similar results have been observed in recent studies examining prognostic scoring methods in severe scrub typhus [23,29].

Another strength of the present study is the inclusion of patients with established MODS who were hospitalized to a tertiary care referral centre. These patients are the subset most at risk of mortality and resource usage. Evaluation of laboratory abnormalities, organ dysfunction, need for vasopressors, and therapeutic response gives clinically meaningful information that may help clinicians to identify early on those high-risk patients who require intense monitoring. In addition, the study provides valuable regional data from Central India, where published evidence regarding scrub typhus associated MODS is very sparse despite the rising incidence of the disease.

However, there are certain limitations to the study. The findings may not be generalizable to other health care settings due to the relatively small sample size and single-centre methodology. Since this was an observational study, we cannot analyze causal links between laboratory abnormalities and clinical outcomes. Delayed complications and long-term functional results could not be assessed since there was no long-term follow-up following discharge from the hospital. In addition, modern molecular diagnostic tools such as polymerase chain reaction (PCR) and genotyping of Orientia tsutsugamushi were not commonly available, which may have constrained the thorough

microbiological characterisation of the infection.

However, in spite of these limitations, the study provides a valuable insight into the clinical spectrum of scrub typhus-associated MODS in Central India. The findings highlight that thrombocytopenia, coagulation abnormalities, respiratory compromise and raised SOFA scores should alert clinicians to the likelihood of severe illness. Early diagnosis, rapid beginning of doxycycline medication, intensive supportive management and serial monitoring of organ dysfunction by SOFA score are vital for improvement of patient outcome. Enhancement in physician awareness, laboratory diagnostic facilities and standardised management protocols at secondary and tertiary healthcare institutes can significantly reduce illness related morbidity and mortality in endemic areas.

CONCLUSION

The present study emphasizes that scrub typhus is a significant but potentially reversible cause of multiple organ dysfunction syndrome. Early diagnosis and effective treatment are the cornerstone for limiting progression to severe disease and enhancing survival. These findings require validation by future multicentric research with bigger patient populations and long-term follow-up to create strong predictive models for early risk stratification in patients with scrub typhus.

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