Section: General medicine

Original Research Article

ASSESSMENT OF A CLINICAL RISK SCORING ALGORITHM FOR SCRUB TYPHUS PROGNOSTICATION

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ABSTRACT

Background: Scrub typhus is an acute febrile illness caused by Orientia tsutsugamushi, endemic in Asia-Pacific regions and associated with significant morbidity and mortality if not recognized early. Clinical features are often nonspecific, leading to delayed diagnosis and complications such as renal failure, ARDS, and shock. Prognostication tools like the Clinical Risk Scoring Algorithm (CRSA) can help identify high-risk patients and guide timely management. **Materials and Methods:** This prospective, non-interventional study was conducted over one year in the Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Puducherry. Fifty patients aged above 15 years with scrub typhus confirmed by card test were included. Demographic, clinical, and laboratory data were collected using a semi-structured proforma. The CRSA was applied to categorize patients into non-severe, severe, and fatal groups. Outcomes were recorded, and statistical analysis was performed using SPSS. **Results:** The mean age of participants was 47.5 years, with a slight female predominance (54%). Based on CRSA scoring, 64% were classified as non-severe, 26% as severe, and 10% as fatal. Significant associations were observed between severity and gender ($p = 0.019$), presence of crepitations ($p = 0.006$), serum albumin ($p = 0.002$), serum creatinine ($p = 0.029$), and blood pressure (systolic $p = 0.013$, diastolic $p = 0.010$). Serum creatinine, age, and pulse rate showed positive correlations with CRSA scores, while serum albumin correlated negatively. **Conclusion:** The CRSA proved to be a useful tool in stratifying scrub typhus patients according to disease severity. Incorporating basic clinical signs and routine laboratory parameters, it can facilitate early risk identification and guide management decisions, potentially improving patient outcomes in endemic regions.

INTRODUCTION

Large regions of South Asia, East Asia, and Southeast Asia are endemic for scrub typhus, an acute febrile illness. East Africa, Chile, and the Middle East have also recorded cases. Meningoencephalitis, acute respiratory distress syndrome, shock, and renal failure are signs of severe disease.[1-5]

The intracellular bacteria of the genus Orientia, of which Orientia tsutsugamushi is the predominant species in Asia,6 are the cause of scrub typhus. The variety of strains of O. tsutsugamushi restricts resistance to reinfection.[7] The bite of trombiculid mite larvae (chiggers), which produce distinctive eschar at the inoculation site, is how Orientia organisms are spread. In Asia, scrub typhus is one of the most common causes of severe fever of undetermined origin, according to hospital-based research.[8]

The illness poses a severe threat to public health across the Asia-Pacific area, which includes but is not limited to the "tsutsugamushi triangle." This triangle region, which spans more than eight million square kilometres and affects over one billion people in nations like Pakistan, Australia, and Japan, presents a serious danger to public health and is very likely to be lethal.[9]

A systematic review analysing the prevalence of scrub typhus in our country, it is part of the

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"tsutsugamushi triangle," 25.3% of acute febrile illness cases are caused by scrub typhus.[10] Scrub typhus remains an overlooked condition concerning research and the formulation of healthcare policies, even though it is one of the prevalent microorganisms that cause this kind of sickness. People of all ages and visitors to endemic areas are at risk of contracting this illness. clinical characteristics often appear as fever, headache, myalgia, and gastrointestinal symptoms develop after 6 - 21 days of incubation. Scrub typhus's distinctive "eschar" usually starts as a primary papular lesion at the bitten site. Later on, however, it will form a crust and develop into a black ulcer with core necrosis. However, each location may have a different eschar presence. Clinical suspicion should be the key determinant for starting treatment, which serological testing should subsequently confirm.

Although the illness is self-limiting, serious complications and a 30% mortality rate might result from a delay in identification and the start of effective treatment. Complications include acute respiratory distress syndrome (ARDS), acute kidney injury, hepatitis, pneumonia, septic shock, jaundice, meningoencephalitis and myocarditis, will effect at variable percentages of patients beyond the first week of sickness.[11] The diagnosis is difficult because symptoms are vague and often mistaken for those of other tropical illnesses, leading to low clinical suspicion. Frequently, the diagnosis is delayed and the severe cases are not identified in time, which results in complications and death.

Therefore, predicting the severity of an illness may aid in identifying people who have it and in the early start of intensive therapy. Numerous other illness, including malaria, clostridium difficile infection, dengue fever, pneumonia, and dengue haemorrhagic fever, already have such prognostication scores. For scrub typhus, a comparable scoring system was just created in Thailand.[12]

A clinical risk-scoring algorithm (CRSA score) was created for estimating scrub typhus severity in 526 patients from different general hospitals in Thailand during the years 2004 - 2010. The algorithm was assessment and validated against a dataset of 257 scrub typhus cases from one of the participating hospitals. Despite being one of the endemic areas, India lacks an algorithm for severe scrub typhus based on its population.[13]

Objectives

To assess the clinical and laboratory findings in a scrub typus patients and grade them according to the clinical risk scoring algorithm.

To make the scoring system and clinical guidelines to improve patient management in the early stages of the disease.

MATERIALS AND METHODS

This was a prospective, non-interventional study conducted in the Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Puducherry. The study was carried out over a period of one year after obtaining approval from the PG Training Research Committee and the Institutional Human Ethics Committee (IHEC).

All participants were recruited after obtaining informed consent. Patients diagnosed with scrub typhus who satisfied the eligibility criteria were enrolled consecutively from the outpatient department and the Emergency Department of the hospital. Adults aged more than 15 years who were diagnosed with scrub typhus by card test were included in the study. Patients with previously diagnosed hematological disorders affecting one or more hematopoietic cell lines such as ITP or pancytopenia, disorders causing deranged liver function such as acute viral hepatitis, ischemic hepatitis or drug-induced hepatotoxicity, seizure disorder, dementia, critically ill patients developing fever during hospital stay, those with end-stage disease including malignancies on palliative treatment, patients receiving chemotherapy or immunosuppressant therapy, and those with advanced HIV disease were excluded.

The sample size was calculated using the formula $n = 4 \times SD^2 / L^2$. Based on a standard deviation of 3.48 obtained from a previous study and an allowable error of 1, the required sample size was calculated as 48.44. Rounding off, a total of 50 patients were included in the study.

Data were collected using a semi-structured proforma that included demographic details, clinical history, and relevant laboratory findings. All eligible patients underwent a detailed clinical assessment, followed by routine and specific laboratory investigations, which included complete hemogram, renal function tests, liver function tests, serum electrolytes, and scrub typhus card test. The laboratory parameters recorded included hemoglobin, total counts, platelet counts, renal and liver parameters, and urine routine analysis. The Clinical Risk Scoring Algorithm (CRSA) was applied to assess disease severity based on predefined criteria, and organ dysfunctions in severe scrub typhus were defined as per standard guidelines.

Clinical Risk Scoring Algorithm (CRSA)

S. No	Name of the dependent / independent variables	CATEGORY	ASSIGNED SCORE
1	Age(in years)	<15yrs >15yrs	0 3
2	Pulse rate (beats per minute)	<100bpm >100bpm	0 2
3	Crepitation	NO YES	0 2
4	Aspartate transaminases (IU/L)	<160IU/lt >160 IU/lt	0 2
5	Serum albumin(g/dl)	<3.0 g/dl >3.0 g/dl	3 0
6	Serum creatinine(mg/dl)	<1.4mg/dl >1.4mg/dl	0 4

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Definition of Organ Dysfunctions in Severe Scrub Typhus

Organ system	CRIETERIA
Cardiovascular system	Presence of any of the following: Systolic blood pressure <90 mm Hg Abnormal cardiac arrhythmias with no previous history of atrial fibrillation, supraventricular tachycardia, premature ventricular contraction. • Myocarditis, elevated creatinine kinase-MB above baseline
Respiratory system	Acute respiratory distress syndrome, defined as PaO2/FiO2 <200 mm Hg, with bilateral interstitial infiltration on chest film with normal cardiothoracic ratio, or no volume overload of central venous pressure from central venous pressure
Central nervous system	Presence of any of the following: Glasgow Coma Scale ≤12 without other causes Seizure without other causes, or • Meningoencephalitis
Haematology	Platelet count ≤20,000/mm3
Urinary tract	Presence of acute renal failure, defined as creatinine ≥2 mg/dL or creatinine change >0.5 mg/dL/day
Gastrointestinal/hepatobiliary tract	Presence of hepatitis, defined as elevated aspartate transaminase or alanine transaminase more than fivefold

Patients were classified according to the CRSA score into three groups: non-severe (CRSA score ≤5), severe (CRSA score 6–9), and fatal (CRSA score ≥10). They were managed by the treating physicians according to their clinical judgment, using either azithromycin or doxycycline. The final in-hospital outcome for each patient was documented. Data were analyzed using SPSS software. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The mean age of the study participants was 47.5 years (SD ±14.47), with the youngest participant being 15 years old and the oldest 74 years. The study population consisted of 54% females and 46% males. The mean pulse rate among participants was 96.66 beats per minute (bpm) (SD ±15.77), with a minimum of 60 bpm and a maximum of 130 bpm.

Table 1: Blood pressure in the study participants

Variable	Mean	SD	Minimum	Maximum
Systolic Blood pressure	118.2	21.35	90	200
Diastolic Blood pressure	73.6	11.74	40	100

The mean systolic blood pressure was 118.2 mmHg (SD ±21.35), with a range of 90–200 mmHg, while the mean diastolic blood pressure was 73.6 mmHg (SD ±11.74), with values ranging from 40–100 mmHg.

Table 2: Laboratory Parameters in the study participants

Variable	Mean	SD	Minimum	Maximum
AST	99.86	128.76	10	755
Serum albumin	3.42	0.48	2.4	4.3
Serum creatinine	1.13	0.86	0.44	5.65
Platelets	183160	99964.35	16000	512000

- Upon physical examination, 18% of participants had crepitations, while 82% did not 88% (44) and 12% (6) of the study participants had aspartate aminotransferase of less 160 IU/lt and more than 160 IU/L respectively. The mean AST level was 99.86 IU/L (SD ±128.76), with values ranging from 10 IU/L to 755 IU/L.
- 16% (8) and 84% (42) of the study participants had serum albumin of less 3.0 g/dl and more than 3 g/dl respectively. The mean serum albumin was 3.42 g/dL (SD ±0.48), with a minimum of 2.4 g/dL and a maximum of 4.3 g/dL.
- 86% (43) and 14% (7) of the study participants had serum creatinine of less.
- 1.4 mg/dl and more than 1.4 mg/dl respectively. The mean serum creatinine was 1.13 mg/dL (SD ±0.86), ranging from 0.44 mg/dL to 5.65 mg/dL.
- 40% (20) and 60% (30) of the study participants had platelets of less 150000 and more than 150000 respectively. The mean platelet count was 183,160 cells/µL (SD ±99,964.35), ranging from 16,000 to 512,000 cells/µL.

Table 3: GCS in the study participants

S No	GCS	Frequency	Percentage
1	3/15	1	2
2	11/15	1	2
3	14/15	1	2
4	15/15	47	94

The majority of participants (94%) had a GCS score of 15/15, while a small percentage had scores of 3/15 (2%), 11/15 (2%), and 14/15 (2%)

Table 4: CRSA in the study participants

S No	CRSA	Frequency	Percentage
1	Non severe	32	64
2	Severe	13	26
3	Fatal	5	10

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The mean CRSA score was 5.26 ± 2.51. Based on the CRSA classification, 64% of participants were categorized as non-severe, 26% as severe, and 10% as fatal.

Table 5: Association between CRSA category and Age

Variable	Non-severe		Severe		Fatal		P value
	Mean	SD	Mean	SD	Mean	SD	
Age	44.72	14.26	50.31	15.55	58.00	6.16	0.098

The mean age of non-severe cases was 44.72 years, while severe and fatal cases had a mean age of 50.31 years and 58.00 years, respectively. However, this difference was not statistically significant (p = 0.098).

Table 6: Association between CRSA category and gender, physical examination in the study participants

Variable	Non-severe		Severe		Fatal		P value
	N	%	N	%	N	%	
Gender							0.019
Female	22	68.8	4	30.8	1	20	
Male	10	31.3	9	69.2	4	80	
Crepitation							0.006
No	30	93.8	9	69.2	2	40	
Yes	2	6.3	4	30.8	3	60	
GCS							0.113
3/15	1	3.1	0	0	0	0	
11/15	1	3.1	0	0	0	0	
14/15	0	0	0	0	1	20	
15/15	30	93.8	13	100	4	80	

Table 7: Association between CRSA category and Pulse rate and Laboratory parameters

Variable	Non-severe		Severe		Fatal		P value
	Mean	SD	Mean	SD	Mean	SD	
Pulse rate	95.22	15.57	93.85	15.07	113.20	10.06	0.036
AST	86.69	98.43	142.92	199.17	72.20	25.43	0.544
Albumin	3.57	0.40	3.25	0.54	2.88	0.24	0.002
Creatinine	0.86	0.22	1.44	1.36	2.04	1.10	0.029
Systolic Blood pressure	118.75	20.75	124.62	22.59	98.00	8.37	0.013
Diastolic Blood pressure	73.44	11.81	78.46	10.68	62.00	4.47	0.010
Platelets	183062.50	95057.86	210307.69	115159.59	113200.00	63915.57	0.105

Table 8: Correlation between variables and CRSA score

	Pearson correlation	P value
Age	0.305	0.031
Pulse rate	0.314	0.026
AST	0.194	0.177
Serum Albumin	-0.397	0.004
Serum Creatinine	0.555	<0.001
Systolic Blood pressure	-0.079	0.588
Diastolic Blood pressure	-0.025	0.861
Platelets	-0.215	0.134

DISCUSSION

The present study was done with the objective to assess the clinical and laboratory findings in a scrub typus patients and grade them according to the clinical risk scoring algorithm.

The present study reported a mean age of 47.5 years (SD: 14.47), with a range of 15 to 74 years, which is compared with multiple studies. Varghese GM et al,[14] observed a mean age of 45 ± 15 years, in Pathania M et al,[15] reported a younger mean age of 30.8 ± 12.3 years. Studies focusing on pediatric cases, such as those by Ganesh R et al,[16] and Kumar M et al.[17] found that the highest burden of disease was among children age between 1 to 5 years. This variation in age distribution across studies suggests differences in regional exposure and population susceptibility.

Gender distribution in the present study showed a little female predominance (54% female, 46% male). However, previous studies have reported mixed trends. Verma SK et al,[18] found a female-to-male ratio of 1.16:1, whereas Kumar M et al,[17] reported a higher prevalence in males (57%). Similar trends were observed in pediatric cases, where Shrestha S et al,[19] documented a higher proportion of female patients (70%), while Ganesh R et al,[16] found a male predominance (male-to-female ratio 1.45:1). These variations may be attributed to occupational exposure, behavioral differences, and healthcare-seeking patterns.

The mean pulse rate in this study was 96.66 bpm (SD: 15.77), consistent with Park et al., who reported a

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mean pulse rate of 94.2 bpm, and Sriwongpan P et al,[20] who identified a pulse rate >100 bpm as a predictor of severe scrub typhus. Pathak S et al,[21] found that 35.5% of scrub typhus patients presented with tachycardia.

Crepitations were observed in 18% of participants, aligning with Kumar M et al,[17] who found a prevalence of 15–20%, and Pathania M et al,[15] who reported pulmonary involvement in 23% of cases. Debnath P et al,[22] documented respiratory symptoms in 35% of cases, further supporting the role of pulmonary manifestations in severe scrub typhus. Cases with pulmonary complications, such as ARDS, have been extensively reported in severe disease presentations (Verma SK et al,[18]).

Liver involvement was evident, as reflected by the mean AST level of 99.86 IU/L (SD: 128.76), with 12% of participants having AST levels above 160 IU/L. Yadav B et al,[23] and Pathak S et al,[21] reported elevated AST levels in 70–88% of patients, while Shrestha S et al,[19] found that 52.5% of cases had elevated SGPT and 26% had elevated SGOT levels. The current findings align with these studies, suggesting mild to moderate transaminitis in most patients.

Serum albumin levels in the present study had a mean of 3.42 g/dl (SD: 0.48), with 16% of participants having levels below 3.0 g/dl. Hypoalbuminemia has been well-documented in scrub typhus, with Sriwongpan P et al.20 identifying albumin ≤3.0 g/dL as a predictor of severity. Pathak S et al,[21] found hypoalbuminemia in 71.1% of patients, while Jakir Hussain S et al,[24] reported low serum albumin in 46.8% of cases. This reduction in albumin levels may be linked to increased vascular permeability and systemic inflammation.

Renal dysfunction was observed, with a mean serum creatinine of 1.13 mg/dl with (SD: 0.86), and 14% of participants had levels above 1.4 mg/dl. Previous studies, including Verma SK et al,[18] and Pathak S et al,[21] have reported AKI in 10–65% of scrub typhus cases. Jakir Hussain S et al,[24] found elevated serum creatinine in 31.9% of patients, while Bansod YV et al,[25] reported renal impairment in 52.1% of cases. This supports the idea that renal involvement is common and can be a marker of severity in scrub typhus.

Blood pressure findings in this study showed a mean systolic blood pressure of 118.2 mmHg (SD: 21.35) and mean diastolic pressure of 73.6 mmHg (SD: 11.74). Hypotension has been well-documented in severe scrub typhus cases, with Liu et al. reporting systolic blood pressure <90 mmHg in critically ill patients. Pathania M et al,[15] documented hypotension in 34% of cases, while Pathak S et al,[21] reported it in 22.4% of cases.

Thrombocytopenia was observed, with 40% of participants having a platelet count below 150,000, and a mean platelet count of 183,160 (SD: 99,964.35). Singh et al. reported similar findings, with platelet counts below 150,000 in 35–45% of cases. Jakir Hussain S et al,[24] found severe thrombocytopenia (<50,000) in 12.8% of cases. Thrombocytopenia in scrub typhus has been linked to bone marrow suppression and immune-mediated destruction.

Neurological involvement was minimal, with 94% of patients having a GCS score of 15/15, and only 6% presenting with lower scores. Studies by Basu S et al,[26] and Pathania M et al,[15] have reported altered sensorium in 5–34% of cases, with seizures documented in 11.8% (Pathak S et al,[21]). Severe cases may develop meningoencephalitis, which has been linked to increased mortality.

The Clinical Risk Scoring Algorithm (CRSA) classified 64% of participants as non-severe, 26% as severe, and 10% as fatal cases, closely mirroring the findings of Sriwongpan P et al.20 where non-severe cases comprised 52.8%, severe cases 27.2%, and fatal cases 20%. Gulati S. et al,[27] validated a similar risk-scoring system and found that a CRSA score ≥7 had a sensitivity of 75.9% and specificity of 77.5% in detecting severe disease.

Further analysis of the CRSA and clinical parameters revealed that older patients were more likely to develop severe disease ($p = 0.098$), strengthening the Sharma et al. and Pathak S et al.[21] Male patients had more severe cases ($p = 0.019$), in agreement with Kumar M et al.[17] The presence of crepitations was significantly associated with severe disease ($p = 0.006$), in line with findings from Pathania M et al,[15] Additionally, low serum albumin ($p = 0.002$) and high creatinine levels ($p = 0.029$) were strongly associated with severe disease, as reported by Kim et al. and Jakir Hussain S et al.[24]

The findings of the present study align closely with existing literature, reinforcing the known laboratory and clinical characteristics of scrub typhus. The associations identified in this study highlight key risk factors for severe disease, emphasizing the importance of early identification and management of high-risk patients to prevent complications and improve outcomes.

CONCLUSION

The CRSA (Clinical Respiratory Severity Assessment) scoring system was central to the present study in categorizing patients based on disease severity into non- severe (64%), severe (26%), and fatal (10%) groups. This stratification revealed key clinical and laboratory patterns across severity levels. A statistically significant association was found between gender and CRSA category ($p = 0.019$), with severe and fatal cases being more prevalent among males. Additionally, participants presenting with crepitations were more likely to fall into the higher severity categories ($p = 0.006$), highlighting the utility of basic clinical findings in predicting disease progression. Although age differences between categories were statistically not significant ($p = 0.098$), the mean age increased with severity, suggesting an age- related trend.

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Several physiological and biochemical parameters showed meaningful associations with CRSA scores. Serum albumin levels were significantly lower in severe and fatal cases ($p = 0.002$), and serum creatinine levels were significantly higher ($p = 0.029$), indicating the contribution of nutritional and renal status to respiratory severity. Pulse rate also increased with severity, being highest in the fatal group ($p = 0.036$), while both systolic and diastolic blood pressures were markedly reduced in this group ($p = 0.013$ and 0.010, respectively), suggesting circulatory compromise. Correlation analysis confirmed that serum creatinine ($r = 0.555$, $p < 0.001$), pulse rate ($r = 0.314$, $p = 0.026$), and age ($r = 0.305$, $p = 0.031$) were positively correlated with CRSA scores, whereas serum albumin was negatively correlated ($r = -0.397$, $p = 0.004$). These findings support the CRSA score as a valuable tool for identifying high-risk patients and guiding clinical decisions in respiratory illness management.

The Clinical Risk Scoring Algorithm (CRSA) proved to be a valuable tool for stratifying patients based on disease severity. By incorporating key clinical and laboratory parameters, CRSA facilitates early risk assessment, enabling timely and targeted interventions. Its application in clinical practice can assist healthcare professionals in prioritizing patients who require intensive monitoring and aggressive management, ultimately improving survival rates and reducing morbidity associated with severe scrub typhus.

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