

Research Article

A Study on Clinical Profile, Inflammatory Markers and Outcome of Scrub Typhus

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ABSTRACT

Background: Scrub typhus is an important re-emerging zoonotic infection and a significant cause of acute febrile illness in India. Delayed diagnosis may result in severe complications, multiorgan dysfunction, and mortality. This study aimed to describe the clinical profile of scrub typhus and evaluate inflammatory markers, prognosis, and outcomes among affected patients.

Methods: A hospital-based prospective observational study was conducted in the Department of General Medicine and Acute Medical Intensive Care Unit at PES Institute of Medical Sciences and Research, Kuppam, from May 2024 to October 2025. Sixty-four adult patients with IgM-positive scrub typhus were enrolled. Demographic characteristics, clinical features, laboratory parameters, inflammatory markers, complications, and outcomes were recorded and analyzed using descriptive statistics.

Results: The mean age of patients was 48 ± 15.1 years, with a predominance of females (78.1%). Fever was the most common presenting symptom (98.4%), followed by cough (51.6%) and breathlessness (26.6%). Eschar was identified in only 6.7% of patients. Elevated inflammatory markers were common, including CRP (73.4%), ESR (53.1%), and procalcitonin levels suggestive of sepsis or septic shock in 28.1% of cases. Hepatic dysfunction was frequently observed, with elevated AST (73.4%), prolonged prothrombin time (73.4%), and hypoalbuminemia (64.1%). Hyponatremia occurred in 53.1% of patients. Major complications included myocarditis (32.8%), liver failure (29.6%), renal failure (29.6%), encephalopathy (23.4%), and pulmonary embolism (21.8%). Elevated inflammatory markers and hypoalbuminemia were significantly associated with mortality. The case fatality rate was 6.25%, while 93.75% of patients recovered and were discharged.

Conclusions: Scrub typhus commonly presents with fever and respiratory manifestations and is frequently associated with elevated inflammatory markers and multiorgan involvement. Early diagnosis, close monitoring of inflammatory markers, and prompt treatment are essential for improving outcomes and reducing mortality.

Keywords: Scrub Typhus, Acute Febrile Illness, Inflammatory Markers, Prognosis, Multiorgan Dysfunction, Mortality.

INTRODUCTION

In India, individuals frequently visit hospitals due to Acute Febrile Illness (AFI). Diagnosing and treating AFI can be difficult, especially in environments with limited resources. Scrub typhus outbreaks documented from several states in India, where it is a major cause of

AFI.¹⁻⁴ Scrub typhus studied in a few areas in Karnataka, primarily focusing on clinical characteristics and serology (Weil-Felix and IgM Enzyme Linked Immunosorbent Assay/ ELISA. However, studies with confirmed diagnosis (by MIF or molecular methods) and patient follow-up to determine the outcome.⁵ O.

tsutsugamushi is the cause of scrub typhus, a reemerging infectious disease that is spread by the biting of trombiculid mite larvae (chiggers), primarily *Leptotrombidium deliense*.^{5, 6} Despite being seen of as a rural disease, it is now more common in metropolitan settings.

Scrub typhus is typically underdiagnosed in India as a result of clinicians' lack of suspicion and the general lack of availability to suitable diagnostic testing.⁷ Case fatalities can reach 30% if diagnosis and treatment are delayed.⁸ Early diagnosis is crucial, and doxycycline treatment, which can be used as a therapeutic test, is inexpensive, generally effective, and produces a dramatic clinical response within 48 hours. Other effective antibiotics include chloramphenicol and azithromycin.³ However, there are currently no vaccinations against scrub typhus, and reports of the rise of antibiotic-resistant strains of *O. tsutsugamushi* may be concerning.^{9,10} Scrub typhus can manifest in a variety of ways, from preclinical to clinically overt (fever, myalgia, headache, stomach pain, lymphadenopathy, hepatosplenomegaly, eschar, etc.) to multiorgan failure and death in instances that are left untreated.¹¹ Even while eschar at the site of a larval mite bite is pathognomonic for scrub typhus, it may not always be visible.⁴ Therefore, distinguishing scrub typhus from other feverish conditions is very difficult for clinicians. Thus, laboratory assistance becomes essential and using serological testing or molecular techniques.¹²

Despite its low specificity and sensitivity, the Weil-Felix test is still the most widely utilised test in environments with minimal resources.¹³ Rapid card tests, ELISA, MIF, immunoperoxidase assay, and other serological assays are examples. Although MIF is regarded as the gold standard, ELISA is practically very helpful.¹⁴ Since antibody levels are low disease earlier, serological approaches are limited in their ability to detect early. Therefore, it is claimed that molecular techniques such as PCR are helpful for early and verified diagnosis.¹⁵ Additionally, strain typing can benefit from PCR-RFLP.^{13, 16} Gilliam, Karp, Boryong, and Kato are the primary serotypes of *O. tsutsugamushi* that have been identified as antigenic strain types. High variation in the 56-kDa type-specific antigen is responsible for the diversity of antigenic strains.¹⁷ Previously, strain types were identified by serologic testing (such as complement fixation and immunofluorescence) based on 56 kDa protein. When RFLP analysis was used later, it also revealed a great deal of

variation in the isolates' digesting patterns.¹⁸ RFLP and immunofluorescence methods, however, have revealed differences that point to a substantial level of genetic diversity among *O. tsutsugamushi* isolates. Currently, strain types are identified using genotyping, which uses a 56-kDa gene for phylogenetic analysis in comparison with prototype and reference strains.¹⁹ In light of this, a thorough investigation of the clinical spectrum, patient outcomes, and laboratory diagnosis using various techniques, such as molecular approaches and serology (Weil-Felix, ELISA, and MIF), is required.

Aims and Objectives: To describe the clinical profile in Scrub typhus patients and to evaluate inflammatory markers, prognosis and outcome in Scrub typhus patients.

MATERIAL AND METHODS

Study Design and Setting

This hospital-based prospective observational study was conducted in the Department of General Medicine and Acute Medical Intensive Care Unit (AMICU) at PES Institute of Medical Sciences and Research (PESIMSR), Kuppam, over a period of 18 months from May 2024 to October 2025.

Study Population and Sampling

The study included all patients aged more than 18 years who were admitted to the medical wards or AMICU and were diagnosed with scrub typhus based on a positive IgM antibody test against the 56-kDa protein of *Orientia tsutsugamushi* by immunochromatographic assay. Purposive sampling was employed, and a total sample size of 64 patients was calculated based on the study by Thakur CK et al.²⁰

Sample Size Calculation

The sample size was calculated using the single population proportion formula:

$$n = \frac{Z_{1-\alpha/2}^2 \times p(1-p)}{d^2}$$

Assuming an expected prevalence of scrub typhus of 12.1% ($p = 0.121$)²⁰, 95% confidence level ($Z = 1.96$), and an absolute precision of 8% ($d = 0.08$), the minimum required sample size was calculated to be 64 participants. Therefore, a total of 64 patients with IgM-positive scrub typhus were included in the study.

Eligibility Criteria

Patients aged above 18 years with laboratory-confirmed scrub typhus were included in the study. Patients with coexisting infections such as dengue, leptospirosis, malaria, or other causes of acute febrile illness were excluded.

Patients with pre-existing chronic renal failure, chronic liver disease, anaemia, known neoplastic disorders, or other significant comorbid conditions that could influence the clinical profile were also excluded.

Data Collection Procedure

After obtaining informed consent, detailed demographic information, occupation, comorbidities, and presenting complaints such as fever, cough, breathlessness, headache, and gastrointestinal symptoms were recorded. A thorough clinical examination was performed, including assessment for pallor, icterus, cyanosis, clubbing, lymphadenopathy, and pedal oedema. Systemic examination was conducted to identify hepatomegaly, splenomegaly, respiratory findings such as rhonchi and crepitations, and other organ involvement.

Approximately 2 mL of venous blood was collected from each participant and sent to the microbiology laboratory for detection of IgM antibodies against *O. tsutsugamushi* using an immunochromatographic test. Patients diagnosed with scrub typhus received standard treatment, including doxycycline or azithromycin as indicated. Depending on disease severity, patients were managed either in the ward or AMICU and were followed until discharge or death.

Investigations

All patients underwent a comprehensive laboratory evaluation, including complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), procalcitonin, liver function tests, renal function tests, serum electrolytes, arterial blood gas analysis, and prothrombin time. Radiological investigations included chest radiography and ultrasonography of the abdomen and pelvis. Clinical outcomes, duration of hospital stay, need for mechanical ventilation, dialysis requirement, complications, and final outcome were documented.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 23.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were summarized using frequencies and percentages, while continuous variables were expressed as mean $\pm$ standard deviation (SD). Appropriate graphical representations, including bar charts, pie charts, histograms, and box plots, were used to describe the distribution of variables.

RESULTS

A Hospital based prospective observational study was conducted on 64 IgM positive Scrub typhus patients admitted in the ward to evaluate Clinical profile, inflammatory markers and outcome of scrub typhus.

Table 1: Socio-demographic variables

Variables	Frequency (n=64)	Percentage
Age group	20-30	7
	30-40	18
	40-50	13
	50-60	12
	>60	14
	Mean age	48 $\pm$ 15.1 Years
Gender	Male	14
	Female	50
Occupation	Farmer/labourer	26
	Home maker	35
	student	03

Mean age of the patients with Scrub typhus was 48 $\pm$ 15.1 Years. Majority of the patients were aged 30 – 40 years i.e., 28.1%. Scrub typhus was affected in 30 – 40 years aged group, followed by > 60 years(21.9%), 40 – 50 years (20.3%), 50 – 60 years (18.7%) and 20 – 30 years (11%). Thus middle aged and elderly are mostly affected with Scrub typhus. Patients with

scrub typhus admitted in the ward were mostly female i.e., 78.1%, while men were 21.9%. Thus female are affected with Scrub typhus than male. Among the patients admitted, 40.6% of the patients were farmers or daily labourers, 54.7% were home makers, and 4.7% were students. As female were more, most of the patients were house wife.

Table 2: Clinical characteristics, comorbidity and examination findings

	Variable	Frequency (n=64)	Percentage
Clinical characteristics (n=64)	Fever	63	98.4
	<7 days	30	47.6
	7-9 days	28	44.
	≥10 days	05	8
	Cough	33	51.6
	Breathlessness	17	26.6
	Vomiting	08	12.5
	Headache	07	11
	Generalised weakness	03	4.7
	Abdominal pain	03	4.7
	Involuntary micturition	01	1.6
	Giddiness	01	1.6
Comorbidity (n=21)	Loose stools	01	1.6
	Hypertension	17	81
	Type 2 Diabetes mellitus	08	38.1
	CAD	03	14.3
	CVA	02	9.5
	COPD	01	4.8
Physical examination (n=15)	Hypothyroidism	01	4.8
	Pedal edema	12	80
	Pallor	08	53.3
Systemic examination (n=28)	Eschar	01	6.67
	Crepitations	21	75
	Tachycardia	08	28.6
	Epigastric tenderness	05	17.8
	Rhonchi	02	7.14
	Prominent carotid pulsations	02	7.14
	Neck rigidity	02	7.14
	Hepatosplenomegaly	02	7.14
	Altered sensorium	02	7.14
	Abdominal distension	01	3.6
	Hypogastric tenderness	01	3.6

Patients with Scrub typhus presented to the hospital with fever in 98.4% of the patients, 51.6% with Cough, 26.6% with breathlessness, while Nausea/Vomiting, headache in 12.55 and 11% respectively. Gastrointestinal symptoms and weakness in less than 5% of the patients. Thus respiratory symptoms were the most common presentation in the patients. Comorbidity was observed in 21 patients constituting 32.8% of patients. Among the patients with comorbidities, 81% patients were having Hypertension, 38.1% have Type 2 Diabetes mellitus, 14.3% with Coronary artery

On physical examination 15 patients constituting 23.4% of patients had physical signs. Among the patients with signs, 80% patients had pedal edema, 53.3% had Pallor, while only 6.67% had Eschar. On systemic examination of patients, only 43.75% of the patients had abnormal findings. Among the 28 patients, bilateral crepts were observed in 75% of patients, Tachycardia in 28.6%, epigastric tenderness in 17.8% of the patients. Respiratory system was most commonly affected system followed by gastrointestinal tract.

Table 3: Distribution of Vitals, CBP and Inflammatory Markers

	Vitals	Frequency/Mean	Percentage
Pulse rate (n=64)	Mean		
	Normal (60 – 100 beats/min)	93.5 ± 17.2	40.6
	Tachycardia >100 beats/min	26	59.4

Respiratory rate (n=64)	Mean Normal 12 – 20 breaths / min Tachypnoea >20 breaths/min	22.1 ± 5.05 33 31	51.6 48.4
Blood pressure N=63	Normal Elevated Stage 1 Stage 2	35 11 07 10	55.5 17.5 11.1 15.9
SPO2	Mean Hypoxemia <95% Normal 95 – 100 %	95.6 ± 3.36% 22 42	34.4 65.6
Complete blood picture findings			
Hemoglobin	Mean Anamia (<11gm/dl) Normal	12.1 ± 1.94 gm/dl 18 46	28.1 71.9
Total blood count	Mean Leucopenia Normal	8.84 X 10 ³ ± 4.03 4 50	6.3 78.2
Platelets	Mean	225 ± 127	
Inflammatory markers findings			
ESR (mm/hr)	Mean Normal (0 – 20 mm/hr) Inflammation/infection (>20mm/hr)	29.1 (23.1 – 35.1) 30 34	46.9 53.1
CPR (mg/ L)	Mean Normal ≤ 6mg/L Inflammation/infection	87.6 (63 – 112) 17 47	26.6 73.4
Procalcitonin (ng/ml)	Mean Normal <0.05ng/ml Low risk of infection (0.05– 0.5ng/ml) Possible sepsis (0.5 – 2ng/ml) Septic shock(>2ng/ml)	2.02(0.26 – 3.78) 23 23 08 10	36 36 12.5 15.6

On recording vital signs, it is observed that Tachycardia was seen in 59.4%, Tachypnoea in 48.4%, elevated blood pressure in 44.5% and Hypoxemia in 34.4% of the scrub typhus patients. Tachycardia is the most common sign observed in the patients. On complete blood picture, 28.1% of the scrub typhus patients had Anaemia. Leucopenia was observed in 6.3% of the patients, while 15.6% of the patients had

Leucocytosis. On evaluation of inflammatory markers, it is observed that through ESR, 53.1% of the patients had suspicion of inflammation or infection. By CRP, 73.4% of the patients confirmed to have inflammation or infection. Through Procalcitonin, it is confirmed that 36% had low risk of infection, 12.5% had Sepsis, 15.6% had Septic shock.

Table 4: Distribution of LFT, RFT, and ABG analysis

Liver function test		Frequency/Mean	Percentage
ALT (Alanine Transaminase / SGPT) -U/L	Mean Normal (7 – 56U/L) Elevated (>56U/L)	67.4(52.9 - 81.9) 39 25	61 39
AST (Aspartate Transaminase / SGOT) - U/L	Mean Normal 10 – 40 U/L Elevated (>40U/L)	76.8(60.2 - 93.5) 17 47	26.6 73.4
ALP (Alkaline Phosphatase): U/L	Mean Normal 44 – 147 U/L Elevated (>147U/L)	134(116 - 152) 22 42	34.4 65.6
Total Bilirubin: mg/dL	Mean Normal 0.3 – 1.2 mg/dL Elevated (>1.2 mg/dL)	1.02(0.67 - 1.36) 51 13	79.7 20.3
Albumin: gm/dl	Mean Normal 3.5 – 5 gm/dl	3.12(2.97 - 3.27) 23.	35.9

	Decreased (<3.5 gm/dl)	41	64.1
Prothrombin Time (PT): 14.4 ± 1.48 S (Mean ± SD)	Mean Normal 11 – 13.5Sec Prolonged >13.5S	14.4 ± 1.48 17 47	26.6 73.4
Renal function tests			
Blood Urea: mg/dL	Mean Reduced (<15 mg/dL) Normal (15 - 40 mg/dL) Elevated/Uremia (>40 mg/dL)	36.6(26.6 - 46.6) 05 49 10	7.8 76.6 15.6
Serum Creatinine: mg/dL	Mean Reduced <0.6 mg/dL Normal 0.6 – 1.2 mg/dL Elevated (>1.2 mg/dL)	0.9(0.73 - 1.08) 08 51 05	12.5 79.7 7.8
Sodium Na+ mEq/L	Mean' Normal 135 – 145 mEq/L Hyponatremia(<135 mEq/L)	134 ± 5.39 30 34	46.9 53.1
Potassium K+ mEq/L	Mean Hypokalemia (<3.5 mEq/L) Normal 3.5 - 5 mEq/L Hyperkalemia (>5 mEq/L)	3.98 ± 0.54 07 53 04	11 82.8 6.2
Chloride Cl- mEq/L	Mean Hypochloremia (< 98mEq/L) Normal 98 - 106 mEq/L Hyperchloremia(> 106 mEq/L)	100 ± 1.59 17 37 10	26.6 57.8 15.6
Arterial Blood Gas analysis			
pH:	Mean Acidosis / Reduced (<7.35) Normal (7.35 – 7.45) Alkalosis / Elevated (>7.45)	7.39 ± 0.06 12 42 10	18.8 65.6 15.6
PaCO2 mm Hg	Mean Hypocapnia<35 mmHg Normal 35 – 45 mmHg Elevated (>45 mmHg)	32.3 ± 5.95 37 25 2	57.8 39.1 3.1
PaO2: mmHg	Mean Hypoxemia<80mmHg Normal 80 - 100 mmHg Elevated (>100 mmHg)	90.5 ± 20.4 12 40 12	18.8 62.4 18.8
HCO3 ⁻ : mEq/L	Mean Reduced <22mEq/L Normal 22 – 26 mEq/L	20 ± 3.3 42 22	65.6 34.4

Liver function tests were done in all the patients with scrub typhus. The observation is as follows

1. ALT was elevated in 39% of patients suggesting liver dysfunction (hepatitis, drug toxicity).
2. AST was elevated in 73.5% of patients suggestive of liver injury.
3. ALP was elevated in 65.6% of patients suggestive of bile duct obstruction or cholestasis; also elevated in bone disease.
4. Total bilirubin was elevated in 20.3% of patients suggestive of jaundice; liver dysfunction, hemolysis, bile duct obstruction.
5. Serum albumin was decreased in 64.06% of patients suggestive of chronic liver disease or poor nutrition.
6. Prothrombin time was prolonged in 73.4% of patients suggestive of impaired liver synthetic function. Thus approximately 60% of patients had liver dysfunction as per liver function tests of patients.

Renal function tests were conducted on all the patients. The results of the test are as follows

1. Blood urea was elevated in 15.6% of the patients suggestive of renal dysfunction, while reduced in 7.8% of patients.

2. Serum creatinine was reduced in 12.5% of patients and elevated in 7.8% of the patients.
3. While assessing serum electrolytes, serum sodium reduced (Hyponatremia) was observed in 53.1% of patients.
4. Hypokalemia was observed in 11% of patients, while hyperkalemia in 6.2%.
5. Hypochloremia was observed in 26.6% and Hyperchloremia in 15.6% of the patients.

Arterial blood gas analysis of all the patients was conducted. The findings are as follows

1. Alkalosis was observed in 15.6% of the patients and acidosis in 18.8% of the patients.

2. Respiratory acidosis was observed in 6 patients i.e., 9.4%.
3. Respiratory alkalosis was observed in 10 patients i.e., 15.6%.
4. Metabolic Acidosis was observed in 8 patients i.e., 12.5%.
5. Hypocapnia was observed in 57.8% of patients.
6. Decreased and elevated PaO₂ was observed in 18.75% of patients each respectively.
7. Reduced HCO₃ was observed in 65.6% of the patients.

Table 5: Distribution of X-Ray findings, USG findings, complications, and outcome

Variable	Frequency (n=64)	Percentage
X ray findings (n=29)	Cardiomegaly	14
	B/L non-homogenous Opacities	10
	Rt Lower lobe Consolidation	07
	Pulmonary edema	02
	Pleural effusion	01
	Early ARDS	01
	ILD	01
USG findings (n=44)	Splenomegaly	22
	Gall bladder edema	09
	Hepatomegaly	08
	Fatty liver	03
	Hydronephrosis	02
	Renal calculi	02
	Hepatosplenomegaly	01
	Ascites	01
	Right adnexal cyst	01
	Polyserosities	01
	ILD	01
Complications	Cardiac dysfunction (myocarditis)	21
	Liver failure	19
	Renal failure	19
	Encephalopathy	15
	Pulmonary embolism	14
	ARDS	9
	Meningitis	9
	DIC	7
	Pneumonia	4
	Peripheral gangrene	3
Outcome	Improved and discharged	60
	Died	04
	Total	64

X ray investigation was done on 29 patients. Out of 29 patients, 48.3% of patients showed

cardiomegaly on X ray, 34.5% with bilateral non homogenous or fluffy opacities, rt lower lobe

consolidation in 24.1%, and pulmonary edema in 6.9% of patients respectively. Ultrasonography was done on 44 patients. Among 44 patients, 50% of the patients showed Splenomegaly. While 20.5% had Gall bladder edema, 18.2% had Hepatomegaly respectively. Other findings involving fatty liver, calculi, adnexal cyst are below 10%. In the study, 32.8% of the patients had Peripheral gangrene, 29.6% of the patients had Liver failure, Renal failure, 23.4% patients had

Encephalopathy, 21.8% had Pulmonary embolism, 14.1% patients had ARDS, Meningitis, 10.9% patients had DIC, 6.2% patients had Pneumonia and 4.6% patients had Peripheral gangrene. Case fatality rate of scrub typhus in the study was 6.25%. Patients died with Septic shock, encephalopathy, massive pulmonary thromboembolism. Among 93.75% of the patients improved, were discharged within a week in 76.7%(n=46), and a week – 14 days in 14 patients(23.3%).

Table 6: Comparison of Mean Inflammatory Marker Values between Early (≤ 7 days) and Late (> 7 days) Discharge Groups among Survivors

Parameter	Early Discharge ≤ 7 days (n=49) Mean $\pm$ SD	Late Discharge > 7 days (n=11) Mean $\pm$ SD
ESR (mm/hr)	26.4 $\pm$ 20.6	38.2 $\pm$ 29.1
CRP (mg/L)	82.7 $\pm$ 88.2	50.2 $\pm$ 65.6
Procalcitonin (ng/mL)	0.51 $\pm$ 1.01	0.79 $\pm$ 1.15
Prothrombin Time (s)	14.2 $\pm$ 1.3	14.9 $\pm$ 1.9
Platelet count ($\times 10^3/\mu\text{L}$)	239.7 $\pm$ 123.6	201.8 $\pm$ 136.0

Table 7: Comparison of Categorical Inflammatory Marker Abnormalities between Early and Late Discharge Groups

Inflammatory Marker Category	Early Discharge ≤ 7 days (n=49) n (%)	Late Discharge > 7 days (n=11) n (%)
ESR elevated (> 20 mm/hr)	24 (49.0%)	8 (72.7%)
CRP elevated (> 6 mg/L)	34 (69.4%)	9 (81.8%)
Procalcitonin elevated (> 0.5 ng/mL)	7 (14.3%)	3 (27.3%)
Prothrombin Time prolonged (> 13.5 s)	36 (73.5%)	8 (72.7%)
Thrombocytopenia ($< 150 \times 10^3/\mu\text{L}$)	10 (20.4%)	5 (45.5%)

The late discharge group showed a higher proportion of elevated ESR (72.7% vs. 49.0%), raised procalcitonin (27.3% vs. 14.3%), and thrombocytopenia (45.5%

vs. 20.4%) compared to the early discharge group, suggesting that persistent inflammatory burden contributes to longer hospital stay.

Table 8: Comparison of Inflammatory Markers between Survivors and Non-Survivors

Inflammatory Marker	Survivors (n=60)	Non-Survivors (n=4)	p-value
Elevated ESR (> 20 mm/hr)	27 (45.0%)	4 (100%)	< 0.0001
Elevated CRP (> 6 mg/L)	21 (35.0%)	4 (100%)	< 0.0001
Elevated Procalcitonin (> 0.5 ng/mL)	32 (53.3%)	4 (100%)	< 0.0001

Decreased Albumin (<3.5 g/dL)	19 (31.7%)	3 (75.0%)	<0.0001
ProlongedPT(>13.5s)	22 (36.7%)	4 (100%)	<0.0001

All inflammatory markers were significantly elevated in non-survivors compared to survivors ($p < 0.0001$ for all parameters), underscoring their value as prognostic indicators in scrub typhus.

DISCUSSION

This hospital-based prospective observational study demonstrates that scrub typhus predominantly affects middle-aged and elderly individuals, with a higher incidence among females. In the current study, Patients with Scrub typhus presented to the hospital with fever in 98.4% of the patients, 51.6% with Cough, 26.6% with breathlessness, while Nausea/Vomiting, headache in 12.55 and 11% respectively. Gastrointestinal symptoms and weakness in less than 5% of the patients. Thus respiratory symptoms were the most common presentation in the patients.

Fever was a common symptom in every patient in the S. Shrestha et al. research. Twenty (50%) of the patients reported headache and retro-orbital pain, either with or without eye redness. Eleven people (27.5%) reported experiencing gastrointestinal symptoms, such as nausea, vomiting, and stomach discomfort, which was dull and confined to the upper quadrant without guarding. Fourteen patients (26%) complained of weakness, malaise, or prostration.²¹

In the Bhowmik, et al study, Fever with chills was found in all patients. Headache, cough, nausea/vomiting, and yellow eyes/urine were present among 71.4%, 62.5%, 58.4%, and 26% of patients, respectively. Pallor, icterus, hepatomegaly, and splenomegaly were present among 19.5%, 28.6%, 20.1%, and 15.6% of patients, respectively. The pathognomonic feature of scrub typhus and Eschar was seen among only 13% of patients.²²

92.8% of febrile patients at Changwon Hospital in Korea had seropositive results, according to Park et al.²³ Septic shock caused hypothermia $< 36^{\circ}\text{C}$ in severe instances, according to Sriwongsoan et al.²⁴ Even though eschar is regarded as a pathological indication, we only discovered it in 11 (27.5%) of the cases.

The incidence ranged from 7 to 80%, according to Kim et al.²⁵ Tsay²⁶ reported 60% and Gurung et al²⁷ from Gorkha, Nepal reported 30%. Remarkably, no eschar was reported in a research conducted in Andra Pradesh, India by Ramyashree et al.²⁸ Risk factors such as habitat,

travel to endemic regions, and occupation may provide a clue to aid in diagnosis instead of the various clinical presentations and skin symptoms.

Co morbidity was observed in 21 patients constituting 32.8% of patients. Among the patients with co morbidities, 81% patients were having Hypertension, 38.1% have Type 2 Diabetes mellitus, 14.3% with coronary artery disease, 9.5% with Cerebro vascular accident, while COPD, Hypothyroidism in 4.8% each.

In the Bhowmik, et al study, the comorbid diseases such as diabetes mellitus and hypertension were seen only among 16.9% and 10.4% of patients, respectively.²²

On physical examination 15 patients constituting 23.4% of patients had physical signs. Among the patients with signs, 80% patients had pedal edema, 53.3% had Pallor, while only 6.67% had Eschar. In Mandal, et al study, 15 (42.9%) patients had Rash, 24 (68.6%) patients had lymphadenopathy, 32 (91.4%) patients had Pallor, 9 (25.7%) patients had edema, 3 (8.6%) patients had Jaundice.²⁹ Varghese et al¹⁷ showed that an eschar was present in 43.5% of patients. Takhar et al²⁰ found the pathognomonic features such as eschar (12%) and lymphadenopathy (18%) were not so common in this study.

Pokhrel et al³⁰ showed pathognomonic eschar was observed in 9.1% patients. Das et al³¹ found hepatosplenomegaly (55.45%), respiratory problems (47.54%), abdominal symptoms (40.59%), eschar (26.74%), rashes (15.84%), altered behavior (9.9%), and lymphadenopathy (2.97%) of cases studied.

According to Pathak et al³², lymphadenopathy (60.5%), hepatomegaly (47.4%), oedema (26.3%), jaundice (26.3%), and splenomegaly (15.8%) were significant clinical symptoms. Nine people, or around 12%, experienced necrotic eschar.

In the JV Shwetha et al. study, 32% of patients showed a rash [Table/Fig-3], 16% had pallor, 8% had icterous, and 4% had eschar, which is indicative of scrub typhus (even after a thorough examination in all instances), including one scar where the eschar scab had peeled off.³³

On systemic examination of patients, only 43.75% of the patients had abnormal findings. Among the 28 patients, bilateral crepts were observed in 75% of patients, Tachycardia in

28.6%, epigastric tenderness in 17.8% of the patients. Respiratory system was most commonly affected system followed by gastrointestinal tract.

In Mandal, et al study, 19 (54.3%) patients had mild hepatosplenomegally (HSM) and 9 (25.7%) patients had moderate HSM, 3 (8.6%) patients had Ascites.²⁹ Das et al³¹ found that hepatosplenomegaly (55.45%), respiratory problems (47.54%), abdominal symptoms (40.59%), eschar (26.74%), rashes (15.84%), altered behavior (9.9%), and lymphadenopathy (2.97%) of cases studied. Pathak et al³² found that clinical signs noticed were lymphadenopathy (60.5%), hepatomegaly (47.4%), edema (26.3%), jaundice (26.3%), and splenomegaly (15.8%). In JV Shwetha et al study, Systemic examination revealed hepatosplenomegaly in 53%, signs of CNS involvement in 39% and pleural effusion in 08% patients.³³

In the current study, on complete blood picture, 28.1% of the scrub typhus patients had Anaemia. Leucopenia was observed in 6.3% of the patients, while 15.6% of the patients had Leucocytosis.

Haematological parameters in the S. Shrestha et al. study revealed that 22 (55%) patients had anaemia, 5 (12.5%) had leucopenia, and 9 (22.5%) had leukocytosis. Thirteen people (32.5%) had thrombocytopenia; five of them (12.5%) had severe thrombocytopenia and needed a transfusion.⁵⁸ In the Bhowmik, et al study, A major number of patients had hemoglobin level <10 g/dL (57.1%) and leukocyte count < 4000/cumm (63.6%).²² In Mandal, et al study, the mean hemoglobin (Hb g %) of patients was 9.9971 ± 0.7846 . We examined that the mean platelet count (in lakhs) of patients was 1.8514 ± 0.8416 and we observed that the mean CRP of patients was 91.3200 ± 37.8739 .²⁹

On evaluation of inflammatory markers, it is observed that through ESR, 53.1% of the patients had suspicion of inflammation or infection. By CRP, 73.4% of the patients confirmed to have inflammation or infection. Through Procalcitonin, it is confirmed that 36% had low risk of infection, 12.5% had Sepsis, 15.6% had Septic shock.

Ramanathan and Yazhini found that C-reactive protein (CRP) was positive in 28% (n=14). Das et al.,¹⁰ found that thrombocytopenia, elevated liver enzymes, and raised CRP were found characteristically.³⁴ Of the 120 patients in the Ashima Jamwal et al. study, 112 patients (93.33%) had increased PCT values (0.05-89.4

ng/mL). Of these 120 patients, 17 had increased PCT values (>10), ranging from 23.3 to 89.4 ng/mL, and 12 (10%) died while in the hospital due to elevated PCT levels (26.5-89.4 ng/mL).³⁵

The average C-reactive protein (CRP) level in the Kamath et al. trial was 10.9 ± 6.3 mg/dL, and the highest level recorded was 23.2 mg/dL.³⁶ Approximately 60% of patients had liver dysfunction as per liver function tests of patients. ALT was elevated in 39% of patients suggesting liver dysfunction (hepatitis, drug toxicity). AST was elevated in 73.5% of patients suggestive of liver injury. ALP was elevated in 65.6% of patients suggestive of bile duct obstruction or cholestasis; also elevated in bone disease. Total bilirubin was elevated in 20.3% of patients suggestive of jaundice; liver dysfunction, hemolysis, bile duct obstruction. Serum albumin was decreased in 64.06% of patients suggestive of chronic liver disease or poor nutrition. Prothrombin time was prolonged in 73.4% of patients suggestive of impaired liver synthetic function.

In the S. Shrestha et al study, Biochemical tests revealed elevated levels of SGPT, 21 (52.5%, N = 40), SGOT, 14 (26%), and ALP, 9 (22.5%). Four (10%) each had high bilirubin and hypoproteinemia. Eleven (27.5%) had hypoalbuminemia.²¹ In the Bhowmik, et al study, Liver enzymes such as AST, ALT, and alkaline phosphatase were raised above normal range in 84.4%, 81.8%, and 75.3% of patients, respectively.²²

In the present study, Blood urea was elevated in 15.6% of the patients suggestive of renal dysfunction, while reduced in 7.8% of patients. Serum creatinine was reduced in 12.5% of patients and elevated in 7.8% of the patients. While assessing serum electrolytes, serum sodium reduced (Hyponatremia) was observed in 53.1% of patients. Hypokalemia was observed in 11% of patients, while hyperkalemia in 6.2%. Hypochloremia was observed in 26.6% and Hyperchloremia in 15.6% of the patients.

In the Bhowmik, et al study, Kidney function tests such as blood urea and Scr were above normal range among 51.9% and 57.1% of patients, respectively.²² According to Pathak et al., 36.9%, 34.2%, and 65.8% of patients had thrombocytopenia, elevated liver enzymes, and elevated creatinine levels, respectively. Myocarditis (72.4%), hypoalbuminemia (71.1%), severe thrombocytopenia (22.4%), renal impairment (65.8%), hyponatraemia

(48.7%), and hepatitis (34.2%) were the most frequent consequences.³²

In the current study, Case fatality rate of scrub typhus in the study was 6.25%. Patients died with Septic shock, encephalopathy, massive pulmonary thromboembolism. Among 93.75% of the patients improved, were discharged within a week in 76.7%(n=46), and a week – 14 days in 14 patients (23.3%).

In the Bhowmik, et al study, Hepatic dysfunction was the most common complication (75.3%) in scrub typhus. Renal dysfunction, multiorgan dysfunction, meningoencephalitis, pneumonitis, and ARDS were some other complications found in 57.1%, 44.2%, 10.4%, 11.7%, and 7.8% of patients, respectively. The percentage of mortality among the patients was found to be 6.5% similar to the current study. The factors significantly linked with a negative prognosis, as indicated by a higher mortality rate, include male gender, pre-hospitalization illness duration exceeding 7 days, presence of diabetes mellitus, Scr levels exceeding 1.5 mg/dL, serum bilirubin levels surpassing 3 mg/dL, systolic blood pressure falling below 90 mmHg, altered sensorium, and the presence of ARDS.

²²

In Mandal, et al study, 4 (11.4%) patients had shock, 20 (57.1%) patients had pneumonia/pneumonitis, 5 (14.3%) patients had meningoencephalitis, 3 (8.6%) patients had acute kidney injury (AKI).²⁹ According to Varghese et al¹⁷ the overall case-fatality rate was 9.0%. 33.7% of patients had signs of acute lung damage, and 29.5% needed ventilator support. Meningoencephalitis, shock, and lung damage are among the potentially fatal side effects of scrub typhus.

The overall prognosis in the present study was favourable, with a case fatality rate (CFR) of 6.25% (4 deaths out of 64 patients). Among survivors, 76.7% were discharged within one week and the remaining 23.3% within 7–14 days, with no patient requiring hospitalisation beyond 14 days. This outcome compares well with CFRs reported in similar Indian studies: 6.5% in Bhowmik et al,²² 6.0% in Philomena J et al. (2016), and 9.0% in Varghese GM et al.¹⁷ The four deaths in the present study occurred due to septic shock with multi-organ dysfunction syndrome, septic encephalopathy, and massive pulmonary thromboembolism-consistent with the severe phenotypes associated with fatal outcomes described in the literature.

Scrub typhus remains an important cause of acute febrile illness with potential multi-organ

involvement. Fever with respiratory manifestations was the most common presentation, while elevated inflammatory markers, hepatic dysfunction, electrolyte abnormalities, and respiratory compromise were frequently observed. Although eschar was uncommon, diagnosis was facilitated by clinical suspicion supported by laboratory investigations. Early recognition, prompt initiation of appropriate therapy, and supportive care resulted in favourable outcomes in most patients, whereas severe complications such as septic shock, encephalopathy, and thromboembolism were associated with mortality. Timely diagnosis and close monitoring of organ function and inflammatory markers are essential to reduce complications and improve patient outcomes. Strengthening community awareness regarding prevention of chigger mite exposure in endemic areas and promoting early diagnosis and treatment may help reduce the burden and complications of scrub typhus.

Conclusions: Scrub typhus commonly presents with fever and respiratory manifestations and is frequently associated with elevated inflammatory markers and multiorgan involvement. Early diagnosis, close monitoring of inflammatory markers, and prompt treatment are essential for improving outcomes and reducing mortality.

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