

# Study of clinical and biochemical profile of scrub typhus in a tertiary care hospital of West Bengal



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## ABSTRACT

**Background:** Humans are accidental hosts in the zoonotic disease Scrub typhus. The disease though widespread in our county, it remains grossly underdiagnosed because of its non-septic clinical manifestations and lack of access to specific laboratory facilities. **Aims and Objectives:** The objective of present study is to evaluate the clinical presentations of Scrub Typhus among the study group. Furthermore, to assess the various laboratory findings in Scrub Typhus cases among the study group is the other objective of this study. **Materials and Methods:** The present study is an Institution-based, observational, and cross-sectional study conducted for 18 months with the admitted patients having 14–70 years of age. Data collected regarding patients' demographic profile, symptoms, clinical findings, laboratory, and radiological findings. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. **Results:** In our study, we found that most of the patients were 14–20 years old and female population was higher. It was found that 34.3% of patients had Eschar, 42.9% of patients had Rash, and 91.4% of patients had Pallor, 8.6% of patients had Ascites, 25.7% had Edema, 8.6% of patients had Jaundice, 11.4% had shock, and 57.1% had pneumonia/pneumonitis. The present study showed that 65.7% of patients had drug response (Doxycycline). **Conclusion:** Knowledge of geographical distribution, evidence of exposure to vector, clinical features such as fever, rash, eschar, headache, and myalgia along with high index of suspicion are crucial factors for early diagnosis and that helps in timely treatment of the cases.

**Key words:** Clinical profile; Eastern India; Scrub typhus

## INTRODUCTION

Scrub typhus, caused by *Orientia tsutsugamushi*,<sup>1</sup> is an acute Infectious disease of variable severity that is transmitted to humans by an arthropod vector of *Trombiculidae* family, affecting people of all ages including children. Humans are accidental hosts in this zoonotic disease. Although the disease is widespread in our county, it remains grossly underdiagnosed because of its non-septic clinical manifestations and lack of access to specific laboratory facilities.<sup>2</sup>

The clinical spectrum of scrub typhus varies from mild-to-moderate severity. Acute fever is the most common manifestation later accompanied by headache, myalgia, and cough. Incubation period varies from 7 to 21 days. The bite of this mite shows a characteristic black Eschar is useful to the doctor for making a diagnosis.<sup>3</sup> Severe complications include prominent encephalitis, interstitial pneumonia and adult respiratory distress syndrome, and circulatory collapse with hemorrhagic features.<sup>4</sup>

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In India, the current serological diagnostic test continues to be immunoglobulin M enzyme-linked immunosorbent assay (IgM ELISA), as the gold standard. Immunofluorescence antibody (IFA) kit is not readily available in the country.<sup>4</sup>

According to the World Health Organization, Scrub typhus is probably one of the most underdiagnosed and under-reported febrile illnesses requiring hospitalization.<sup>3,4</sup> In India also, it is a neglected disease. The mortality of the disease varies from 7% to 30%.<sup>5</sup>

In India, every year during and after monsoon season, there is sudden rise in cases of acute febrile illness. Viral infections, malaria, dengue, typhoid, leptospirosis and scrub typhus have been classically responsible for such outbreaks.<sup>1</sup> These diseases present with overlapping clinical features.<sup>2</sup> This often leads to either misdiagnosis or delay in diagnosis.

This study will provide diagnostic clues to the primary care physicians, so that they can diagnose cases of scrub typhus earlier for better outcome of patients.

### Aims and objectives

The objective of present study is to evaluate the clinical presentations of Scrub Typhus among the study group. Furthermore, to assess the various laboratory findings in Scrub Typhus cases among the study group is the other objective of this study.

## MATERIALS AND METHODS

The present study is an institution-based, observational, and cross-sectional study and it is carried out in Medicine wards of a government run medical college of West Bengal, eastern part of India. The study was conducted for 18 months with the admitted patients having 14–70 years of age. The study group consists of patients diagnosed with scrub typhus in medicine ward, who had given informed consent for the study.

### Inclusion criteria

Patients admitted in medicine ward who were tested positive for IgM Antibody against *O. tsutsugamushi* by ELISA during the study period were included in the study.

### Exclusion criteria

Those who had not given Informed consent to participate in this research. Patients diagnosed to have some other associated infection and other causes of acute febrile illness are excluded from this study.

Study tools include history, bed head ticket, clinical examination, blood reports, and radiological reports.

Target sample size of 30 (from the previous records) cases is considered.

Data collected regarding patients' demographic profile, symptoms, clinical findings, laboratory, and radiological findings. Data collected in the proforma were collated in MS Excel and analyzed statistically using SPSS software version 27.0.

Ethical clearance had been taken from Medical college authority (IEC Registration: No/NMC/687 Dated: February 10, 2020.)

Statistical analysis done as the data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Z-test (Standard Normal Deviate) was used to test the significant difference of proportions. Once a t-value is determined, a P-value can be found using a table of values from Student's t-distribution.  $P \leq 0.05$  was considered for statistically significant.

## RESULTS

Result and analysis are presented in tabulated manner underneath.

## DISCUSSION

Total 35 patients were present in this study. The present study tables show that in our study, 9 (25.7%) patients were 14–20 years of age, 7 (20.0%) patients were 21–30 years of age, 7 (20.0%) patients were 31–40 years of age, 7 (20.0%) patients were 41–50 years of age, and 5 (14.3%) patients were 51–70 years of age. We observed that, in our study, 20 (57.1%) patients were Female and 15 (42.9%) patients were Male (Table 1).

Rathi and Rathi<sup>6</sup> found that failure of timely diagnosis leads to significant morbidity and mortality. With timely diagnosis, treatment is easy, affordable and often successful with dramatic response to antimicrobials. Antimicrobials effective for Rickettsial disease is usually not included in empirical therapy of nonspecific febrile illnesses, treatment of rickettsia disease is not provided unless they are suspected.

Varghese et al.,<sup>7</sup> showed that the most common presenting symptoms were fever (100%), nausea/vomiting (54%), shortness of breath (49%), headache (46%), cough (38%), and altered sensorium (26%). An eschar was present in 43.5% of patients. Common laboratory findings included

elevated transaminases (87%), thrombocytopenia (79%), and leukocytosis (46%). The overall case-fatality rate was 9.0%. Features of acute lung injury were observed in 33.7%, and 29.5% required ventilatory support. Scrub typhus can manifest with potentially life-threatening complications such as lung injury, shock, and meningoencephalitis.

Takhar et al.,<sup>5</sup> found that fever was the most common presenting symptom (100%), and in 67% its duration was for 7–14 days. Other symptoms were breathlessness (66.7%), haemoptysis (63.6%), oliguria (51.5%), and altered mental status (39.4%). The pathognomonic features such as eschar (12%) and lymphadenopathy (18%) were not so common in this study.

Pokhrel et al.,<sup>8</sup> showed that among the 154 patients, the most common symptoms were fever (100%), headache (79.2%), sweating (70.1%), breathing difficulty (51.3%), redness of the eye (43.5%), and pathognomonic eschar was observed in 9.1% patients.

Das et al.,<sup>9</sup> found that fever was present in all cases and about 81.19% of children presented with fever for more than 7 days. Other findings were 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 al.,<sup>10</sup> found that scrub typhus (n=76) presented with fever and commonly had other symptoms such as headache (75%), myalgia (68.4%), vomiting (64.5%), nausea (59.2%), abdominal pain (57.9%), cough (35.5%), shortness of breath (22.4%), altered sensorium (14.5%), rashes (13.2%), and seizures (11.8%). Important clinical signs noticed were lymphadenopathy (60.5%), hepatomegaly (47.4%), edema (26.3%), jaundice (26.3%), and splenomegaly (15.8%). About 12% (n=9) had necrotic Eschar. Similarly, thrombocytopenia, raised liver enzymes, and raised creatinine values were seen in 36.9%, 34.2% and 65.8%, respectively. The most common complications were myocarditis (72.4%), hypoalbuminemia (71.1%), severe thrombocytopenia (22.4%), renal impairment (65.8%), hyponatremia (48.7%), and hepatitis (34.2%). Over two-thirds (69.70%) of the cases were treated with doxycycline followed by combination with azithromycin in the remaining 18.4%.

We examined that 12 (34.3%) patients had Eschar. Here, the value of z is 2.6295 and  $P=0.00854$  which is significant at  $P<0.05$  (Table 2).

Our study showed that 15 (42.9%) patients had Rash (Table 2).

Data of our study showed that 24 (68.6%) patients had lymphadenopathy (Table 2).

We observed that 32 (91.4%) patients had Pallor. The value of z is 6.9323 and the value of  $P<0.00001$  which is significant at  $P<0.05$ .

The present study also showed that 19 (54.3%) patients had mild hepatosplenomegally (HSM) and 9 (25.7%) patients had moderate HSM (Table 2). Here, the value of z is 2.4398 and the value of  $P=0.01468$  that is significant at  $P<0.05$ .

Our study showed that 3 (8.6%) patients had Ascites (Table 2). Here, the value of z is 6.9323, the value of  $P<0.00001$  which is significant at  $P<0.05$ .

Data of our study showed that 9 (25.7%) patients had edema (Table 2). Where the value of z is 4.0638, the value of  $P<0.00001$  which is significant at  $P<0.05$ .

We observed that, 3 (8.6%) patients had Jaundice (Table 2). Here, the value of z is 6.9323, the value of  $P<0.00001$  which is significant at  $P<0.05$ .

Takhar et al.,<sup>5</sup> found that the most common radiological observation was consistent with acute respiratory distress syndrome. Complications noted were respiratory (69.7%), renal (51.5%), and hepatic dysfunction (48.5%). The overall mortality rate was 21.2%.

We examined that 4 (11.4%) patients had shock, the value of z is 6.4542 and the value of  $P<0.00001$  which the result is significant at  $P<0.05$ .

Our study showed that 20 (57.1%) patients had pneumonia/pneumonitis, the value of z is 1.1952 and the value of  $P=0.23014$  which is however not significant at  $P<0.05$ .

The present study showed that 5 (14.3%) patients had meningoencephalitis, the value of z is 5.9761 and the value of  $P<0.00001$  which is significant at  $P<0.05$  (Table 5).

We observed that 3 (8.6%) patients had acute kidney injury (AKI), the value of z is 6.9323 and the value of  $P<0.00001$  which is significant at  $P<0.05$ .

Peesapati et al.,<sup>11</sup> found that there was a dramatic response to doxycycline in nearly all the patients. It should be considered as an important differential diagnosis in a

febrile patient with thrombocytopenia, deranged liver, or renal functions.

We found that 23 (65.7%) patients had drug response (Doxycycline), the value of  $z$  is 2.6295 and the value of  $P=0.00854$  which is significant at  $P<0.05$ .

Baruah et al.,<sup>12</sup> found that fever was the most common symptom (100%), followed by altered sensorium (63.15%).

Our present study showed that the mean duration of fever (days) on admission of patients was  $8.5429\pm 1.6863$  (Table 4).

Ramanathan and Yazhini<sup>13</sup> found that normal leukocyte count was seen in 48% ( $n=24$ ) of the cases, leukocytopenia 30% ( $n=15$ ), and leukocytosis 22% ( $n=11$ ). Platelets  $<1.5$  lakhs were seen in 72% ( $n=36$ ) and none of the cases had platelets  $<80000$ . Hb  $<9$  g/dL was seen in 44% ( $n=22$ ). Hyponatremia was seen in 24% ( $n=12$ ). C-reactive protein (CRP) was positive in 28% ( $n=14$ ). Hypoalbuminemia was seen in 22% ( $n=11$ ). Renal function test was normal in all the cases. This study discusses the various biochemical and hematological changes in patients with Scrub typhus. However, Pokhrel et al.,<sup>9</sup> found that 50% of scrub typhus patients had low platelet count and more than 30% of patients had an elevated level of liver enzymes (such as serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase (SGOT)). Das et al.,<sup>10</sup> found that thrombocytopenia, elevated liver enzymes, and raised CRP were found characteristically. Defervescence after starting doxycycline was within  $3.26\pm 2.26$  days. Scrub typhus can present in various ways but mostly with prolonged fever.

Sivaprakasam et al.,<sup>14</sup> found that the factors for predicting severity in scrub typhus were hemoglobin  $<10$  g/L, platelet  $<150\ 000$  cells/mm<sup>3</sup>, albumin  $<2.5$  g/d, SGOT  $>5$  fold rise, prolongation of PT, and altered sensorium were correlated with severe disease.

Sandhu et al.,<sup>15</sup> found that hemoglobin, platelet count, and serum albumin were considerably lower in patients who died, whereas AST, serum urea, and creatinine were higher in them. Lower levels of hemoglobin, platelet count, serum albumin and higher levels of total leukocyte count, hepatic transaminases, and serum creatinine correlated with severity.

Data of our present study showed that the mean hemoglobin (Hb g %) of patients was  $9.9971\pm 0.7846$ . We examined that the mean platelet count (in lakhs) of patients was  $1.8514\pm 0.8416$  and we observed that the mean CRP of patients was  $91.3200\pm 37.8739$ . Our study

(Table 3) also showed that the mean AST of patients was  $54.1714\pm 39.0704$ . We examined that the mean ALT of patients was  $56.5714\pm 45.7694$ . It was found that the mean PT-INR of patients was  $0.8286\pm 0.2270$  in our study.

**Table 1: Distribution of age and sex for the disease**

Variable	Subgroup (years)	Frequency	Percentage
Age	14–20	9	25.7
	21–30	7	20.0
	31–40	7	20.0
	41–50	7	20.0
	51–60	5	14.3
	61–70	0	0
	Total	35	100.0
Sex	Female	20	57.1
	Male	15	42.9
	Total	35	100.0

**Table 2: Distribution of clinical variables**

Clinical variable	Presence/absence	Frequency	Percentage
Escher	Absent	23	65.7
	Present	12	34.3
	Total	35	100.0
Rash	Absent	20	57.1
	Present	15	42.9
	Total	35	100.0
Lymphadenopathy	Absent	11	31.4
	Present	24	68.6
	Total	35	100.0
Pallor	Absent	3	8.6
	Present	32	91.4
	Total	35	100.0
HSM (Hepatosplenomegally)	Absent	7	20.0
	Mild	19	54.3
	Moderate	9	25.7
	Total	35	100.0
Ascites	Absent	32	91.4
	Present	3	8.6
	Total	35	100.0
Edema	Absent	26	74.3
	Present	9	25.7
	Total	35	100.0
Jaundice	Absent	32	91.4
	Present	3	8.6
	Total	35	100.0
Shock	Absent	31	88.6
	Present	4	11.4
	Total	35	100.0
Pneumonia	Absent	15	42.9
	Present	20	57.1
	Total	35	100.0
Meningoencephalitis	Absent	30	85.7
	Present	5	14.3
	Total	35	100.0
Acute kidney injury	Absent	32	91.4
	Present	3	8.6
	Total	35	100.0
Drug response (doxycycline)	No	12	34.3
	Yes	23	65.7
	Total	35	100.0

**Table 3: Distribution of hematology and biochemical reports**

Variables	Number	Mean	SD	Minimum	Maximum	Median
TLC	35	12660.0000	5425.8206	5300.0000	33600.0000	12500.0000
Neutrophil (%)	35	49.4000	17.1210	18.0000	76.0000	50.0000
Hb	35	9.9971	0.7846	8.1000	11.2000	10.0000
Plt Count (in lakhs)	35	1.8514	0.8416	0.5000	4.5000	1.7000
CRP	35	91.3200	37.8739	45.0000	178.0000	78.0000
AST	35	54.1714	39.0704	12.0000	182.0000	65.0000
ALT	35	56.5714	45.7694	12.0000	201.0000	63.0000
PT-INR	35	0.8286	0.2270	0.6000	1.6000	0.8000
creatinine	35	0.9506	0.2652	0.6000	1.9000	0.9000
Scrub IgM (ELISA)	35	2.1312	0.3342	1.2320	2.6320	2.1470

TLC: Total leucocyte count, Hb: Hemoglobin, Plt: Platelet count in lakhs, PT-INR: Prothrombin time, International normalized ratio, CRP: C reactive protein, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

**Table 4: Distribution of duration of fever on admission**

Number of days	Number of cases	Mean	SD	Minimum (day)	Maximum (day)	Median
Duration of fever on admission	35	8.5429	1.6863	6.0000	13.0000	8.0000

In above table showed that the mean duration of fever on admission (mean±SD) of patients was 8.5429±1.6863

**Table 5: CSF study**

Variable	Number of cases	Mean	SD	Minimum	Maximum	Median
CSF Protein (mg/dL)	5	109.6000	27.0703	78.0000	150.0000	102.0000
CSF glucose (mg/dL)	5	64.5000	11.1243	54.0000	80.0000	60.5000
ADA (unit/dL) (adenosine deaminase)	5	3.3000	1.0488	1.5000	4.2000	3.6000

In above table showed that the mean CSF Protein (mean±SD) of patients was 109.6000±27.0703. In above table showed that the mean glucose (mean±SD) of patients was 64.5000±11.1243. In above table showed that the mean ADA (mean±SD) of patients was 3.3000±1.0488

Pathak et al.,<sup>11</sup> found that scrub typhus was diagnosed with IgM ELISA. All cases of scrub typhus (n = 76) presented with fever and commonly had other symptoms.

Thapa et al.,<sup>16</sup> found that fever was common clinical symptom. Thrombocytopenia was seen in 73.7% and raised transaminase aspartate aminotransferase, 76.1% among seropositive cases. Weil-Felix test positive were 22.1%, and IgM ELISA positive were 29.2%.

Chauhan et al.,<sup>17</sup> found that many researchers have reported the profile of scrub typhus from various parts of India with diagnosis based on IgM ELISA. They report here results of a retrospective analysis of IgM positive adult patients with scrub typhus showing eschar as a marker of severe rickettsiosis.

The present study showed that the mean creatinine of patients was 0.9506±0.2652 and in our study the mean Scrub IgM (ELISA) of patients was 2.1312±0.3342.

#### Limitations of the study

In spite of every sincere effort, our study has lacunae. The notable short comings of this study are small sample size and it is a single-center-based study. The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out also.

## CONCLUSION

In our study, 25.7% of patients were 14–20 years of age, 20.0% of patients were 21–30 years of age, 20.0% of patients were 31–40 years of age, 20.0% of patients were 41–50 years of age, and 14.3% of patients were 51–70 years of age. We found that most of the patients were 14–20 years old. In our study, female population was higher than the male population. It was found that 34.3% of patients had Eschar, 42.9% of patients had Rash, 68.6% had and 91.4% of patients had Pallor. We observed that more patients had mild HSM, 8.6% patients had Ascites, 25.7% had Edema, 8.6% of patients had Jaundice, 11.4% had shock, and 57.1% had pneumonia/Pneumonitis. The present study showed that 65.7% of patients had drug response (Doxycycline).

Hence, we conclude that the common symptoms are fever, Eschar Rash, Lymphadenopathy, and Pallor. We observe that more patients had mild HSM, edema, and pneumonia/pneumonitis.

Lower levels of hemoglobin, platelet count, serum albumin, and higher levels of total leucocyte count, hepatic transaminases, CRP, and serum creatinine correlated with Scrub Typhus which can help in early diagnosis of Scrub

Typhus. Scrub typhus has emerged as an important cause of febrile illness with varying clinical manifestations with or without eschar. Knowledge of geographical distribution, evidence of exposure to vector, clinical features like fever, rash, eschar, headache, and myalgia along with high index of suspicion are crucial factors for early diagnosis and timely treatment.

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### Author's Contribution:

**RM**- Literature survey, implementation of study protocol, and data collection; **SGB**- Concept, design, clinical protocol, and manuscript preparation; **AiS**- Statistical analysis and interpretation; **UB**- Review manuscript, editing, manuscript revision, and submission of article; **AJS**- Definition of intellectual content, coordination, and manuscript revision.

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