

## A single-centre experience of scrub typhus in a tertiary care centre - a re-emerging infection

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**Background:** Scrub typhus is a documented disease in Himachal Pradesh, but there have been few clinico-epidemiological studies in this area. The present study is done with IgM ELISA as a diagnostic test which has higher sensitivity and specificity as most of the previous studies had used Weil Felix test as a diagnostic test. **Methodology:** This was a prospective observational study. All the patients more than 18 years of age with positive IgM ELISA for scrub typhus with/without eschar were included. The clinical profile was observed. IgM scrub typhus was done by ELISA. **Results:** Total of 39 patients were observed between July 2016 to Dec 2016. Maximum patients were observed in August, September, and October. Fever with Headache was the most common presenting complaint. Eschar was present in 10 % patients. Complications were seen in 76.92 %. The mortality rate was 0 %. **Conclusion:** The varied presentations and high rate of complications require a high index of suspicion for Scrub Typhus. The general physicians should be sensitized for the early diagnosis and treatment to reduce morbidity and mortality.

**Keywords:** Scrub Typhus, Eschar, Orientia tsutsugamushi, Acute febrile illness

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Debananda Sahoo, Assistant Professor, Department of Internal Medicine, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India. Email: <a href="mailto:drdebanandasahoo@gmail.com">drdebanandasahoo@gmail.com</a>	Sahoo D, Maikap D, Mohanty L, Patro S, Panda SS, Mohanty AP. A single-centre experience of scrub typhus in a tertiary care centre - a re-emerging infection. Int J Med Res Rev. 2020;8(1):57-62. Available From <a href="https://ijmrr.medresearch.in/index.php/ijmrr/article/view/1101">https://ijmrr.medresearch.in/index.php/ijmrr/article/view/1101</a>	

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## Introduction

Scrub typhus is highly under-diagnosed because of its varied and nonspecific clinical presentation, less access to specific diagnostic modalities in most of the areas, and less index of suspicion by the clinicians even if its high endemicity in our country. Its presentation varied from a nonspecific febrile illness with constitutional symptoms like fever, rash, myalgias and headache to a disease process manifesting with multiple organ dysfunctions involving various organs such as kidney (acute renal failure), liver (hepatitis), lungs (acute respiratory distress syndrome), central nervous system (meningitis), or with circulatory collapse with haemorrhagic features. The causative organism for Scrub typhus is *Orientia tsutsugamushi* (*Rickettsia tsutsugamushi*). In India, Scrub typhus and other Rickettsial diseases have been present since very long duration. It was more prevalent in Southeast Asia During World War II, having a major contribution towards morbidity and mortality but the incidence was declined considerably in the later decades and was believed to have disappeared from many parts of India. However, there is a resurgence of scrub typhus in several parts of India, including South India, supported by various recent reports. There are many epidemics of scrub typhus which have been reported from North, East and South India [1-9]. There are few case reports of scrub typhus from Odisha in the literature, though the cases sporadically recently with a rising tendency in incidence are commonly encountered. As the clinical diagnosis is difficult and there is lack of laboratory methods for diagnostic aid in many areas, the public health importance of this disease is underestimated. The incubation period of Scrub typhus ranges from 6 to 21 days with a characteristic presentation of high-grade fever (103-105°F) associated with other symptoms like headache, Nausea/Vomiting, cough, myalgia, conjunctival suffusion and gastrointestinal symptoms. An eschar at the site of tick bite associated with regional lymphadenopathy and a maculopapular rash helps in the diagnostic process. Mortality rates is high among untreated patients ranging from 0-30% and varied depending on the patient's age and region of infection. If other severe complications such as ARDS/Meningitis arise, mortality may still be higher. Most of the time, scrub typhus associated with various complications increasing the fatality rate. Various common complications associated with scrub typhus are hepatitis, acute kidney injury, meningoencephalitis,

Myocarditis, ARDS and septic shock. In spite of the availability of effective treatment in the form of doxycycline, azithromycin, a large number of patients develops complication with high mortality mostly because of delay in the diagnosis and late initiation of specific treatment [10]. In Odisha, there were very few clinico-epidemiological studies regarding scrub typhus is present. So, this prospective observational study was planned in one tertiary care centre of eastern India to provide knowledge regarding various aspects of scrub typhus in adults. The present study was done with IgM ELISA as a diagnostic test as it has better sensitivity and specificity.

## Material and Methods

**Setting:** This was a tertiary care hospital-based study in the department of General Medicine, KIMS, Bhubaneswar, Odisha.

**Type of study and Duration:** a prospective observational study over a period of 6 months ranging from July 2016 to Dec. 2016.

**Sample Size calculation:** Considering of prevalence of Scrub typhus in the localities from recent past studies with a confidence interval of 95% and margin of error of 5%, the sample size calculated to be as 37.44, so total number of patients taken were 39.

**Inclusion criteria:** All patients with acute febrile illness above 18 years of age admitted in the IPD with the diagnosis of Scrub Typhus with or without having an eschar.

Diagnosis of scrub typhus has been made on the basis of the following.

01. Fever with Eschar and IgM ELISA positive for Scrub Typhus
02. Fever without Eschar and IgM ELISA positive for Scrub Typhus along with the response to doxycycline.

**Exclusion Criteria:** Patients having other associated infection. Patient with other co-morbid conditions like chronic renal failure, chronic liver disease, any neoplastic disease etc.

**Data collection:** The clinical profile was observed and recorded using a detailed history of symptoms, recreation, agricultural activities, travel to endemic areas, any treatment record before admission to this hospital and a detailed physical examination and the treatment outcome were noted. Supportive

Investigations like complete blood count, urine routine and microscopy, renal function test, hepatic function test, bleeding time, clotting time, PT/INR, rapid diagnostic test for malaria, peripheral blood smear for malarial parasites, *Leptospira* IgM for Leptospirosis, Widal test, serological test for dengue and blood culture were done. For scrub typhus, IgM antibodies detection was done by qualitative ELISA in serum. Radiologically chest X-ray, Ultrasonography abdomen and pelvis, and CT brain or MRI brain were done wherever indicated. If lymphadenopathy was present, fine needle aspiration cytology was done. For the diagnosis of associated complication and for the ease of comparison, the same standard definitions were used as of other studies on scrub typhus [11].

**“Multiple-organ dysfunction syndrome (MODS):** Dysfunction of more than one organ, requiring intervention to maintain homeostasis.

**Acute kidney injury:** A rise in serum creatinine of more than 1.6 mg/dl or urine output less than 400 ml/24 hrs failing to improve after adequate rehydration.

**Acute respiratory distress syndrome (ARDS):** Bilateral alveolar or interstitial infiltrates on chest radiograph and PaO<sub>2</sub>/FiO<sub>2</sub> less than or equal to 200 mmHg.

**Hepatitis:** Rise in SGOT and SGPT of more than three times the upper normal limit and/or elevation of serum bilirubin > 3 times the upper limit of normal value.

**Pancreatitis:** Rise in threefold or more above the normal level of serum amylase and serum lipase level with typical pain upper abdomen of pancreatitis or radiological evidence of pancreatic involvement.

**Meningitis:** Altered sensorium with the feature of meningeal irritation like neck rigidity, positive Kernig’s sign with elevated protein and/or polymorphic leucocytosis on CSF analysis.

**Disseminated intravascular coagulation (DIC):** was defined as a clinical manifestation of bleeding along with thrombocytopenia and elevated coagulation profile (raised fibrin degradation products, prolonged prothrombin time/INR, activated partial thromboplastin time-aPTT): Platelet count < 80,000/L or 50% decrease in platelet count from the highest value recorded over previous 3 days.

**Myocarditis:** Myocarditis was defined as the presence of systolic global left ventricular wall motion abnormalities on 2D echocardiography along with ECG changes and clinical findings consistent with left ventricular dysfunction in a previously normal individual.

**Shock:** Systolic blood pressure of < 90 mm Hg for at least 1 h despite adequate fluid resuscitation was labelled as a shock.”

All patients who were diagnosed as scrub typhus or having strong clinical suspicion for scrub typhus were treated with doxycycline in the dose of 100 mg twice daily PO for 10 days unless there is any contraindication. Where doxycycline could not use, azithromycin in a dose of 500 mg once daily for 5 days was given. As per requirement, other supportive measures like haemodialysis, mechanical ventilation, blood transfusion, inotropic agent etc. were given where ever required.

**Data analysis:** Statistical analysis was done with SPSS version 19. Statistically significant level was taken at  $p \leq 0.05$  with a confidence interval of 95%. All results are compiled in an excel sheet. Frequency distribution was calculated as a percentage.

**Ethical clearance:** Ethical clearance was obtained from the Ethics Committee of the institution prior to starting the study.

## Results

This study included a total number of 39 patients of proven scrub typhus, admitted in the Medicine ward in Kalinga Institute of Medical Sciences, Bhubaneswar between July 2016 to December 2016. Patients with positive IgM ELISA report for scrub typhus were only included and observed. Out of the 39 patients 17 were females (43.58 %) and 22 were males (56.42%). Majority of the patients (30) were associated with agricultural works (76.92%), either directly or indirectly, among whom males are predominant (60%). Demographic profile of the patients can be seen in Table 1. In the current study the number of cases started rising in July 6(15.38%), peaked in August 12(30.77%) and September 15(38.46%), and declined thereafter in October 4 (10.25 %) and depicted graphically in Figure 1. 33(84.61%) of all our cases occurred in three months of peak rainy season and only 16% cases occurred during rest of year which is statistically significant ( $p = .000$ ).

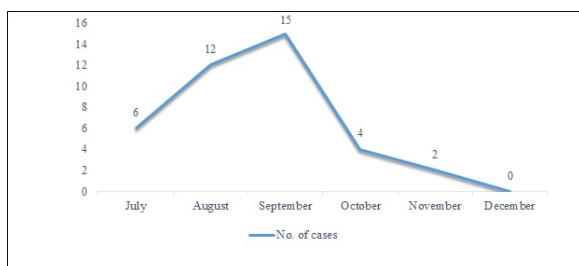
**Table-1: Demographic profile of the patients.**

Variable	Total N=39 (%)	Female N=17(%)	Male N=22 (%)
Sex	39 (100%)	17 (43.58%)	22 (56.42%)
Occupation- Farmers	30 (76.92%)	12 (40%)	18 (60%)
Others	9 (23.08%)	5 (55.55%)	4 (44.45%)

Fever was the main complaint, present in all 39 (100%) patients followed by headache 12(30.76%), shortness of breath 7(17.94%), vomiting 30(76.92%), cough 9(23.07%), altered sensorium 4(10.25%), decreased urine output 10(25.64%) among patients (Table 2). At the time of admission clinical signs noted were hypotension 6(15.38%), icterus 32(82.05%), eschar 3(7.69%), skin rash 3(7.69%). In the present study the eschar was found in 7.69% of the patients which was very low in comparison to 41.7%, 46% from studies done by Dass et al at Meghalaya [12] and M. Vivekanandan et al study [1] at Pondicherry, while most studies of the Oriental countries had eschar in 60-70% patients. The probable explanation for the less frequency of eschar in our area i.e. India specifically in Odisha is variation in cutaneous immunity as well as dark skin of the patients. The active search must be carried out to find the eschar at unusual locations, as this is a painless lesion.

**Table 2: Signs and symptoms at presentation.**

Variable	Total N=39 (%)	Female N=17(%)	Male N=22 (%)
Fever	39 (100%)	17 (100%)	22 (100%)
Cough	9 (23.07%)	4 (23.52%)	5 (22.72%)
Shortness of breath	7 (17.94%)	3 (17.64%)	4 (18.18%)
Altered sensorium	4 (10.25%)	1 (5.88%)	3 (13.63%)
Decreased urination	10 (25.64%)	4 (23.52%)	6 (27.27%)
Headache	12 (30.76%)	4 (23.52%)	8 (36.36%)
Vomiting	30 (76.92%)	14 (82.35%)	16 (72.72%)
Rash	3 (7.69%)	0 (0%)	3 (13.63%)
SBP≤90 mm Hg	6 (15.38%)	2 (11.76%)	4 (18.18%)
Eschar	3 (7.69%)	0 (0%)	3 (13.63%)



**Fig-1: Seasonal Disease Trend**

Complications rates were also quite high among the patients, the most common complication being hepatic dysfunction with 82.05% of patients were having, followed by ARDS (53.84%) and MODS (48.71%). The other common complications which were developed in our patients were renal dysfunction (25.64%) and features of sepsis (25.64%). 15.38% of patients came with septic shock (Table 3).

**Table-3: Complications of Scrub Typhus.**

	Total N=39 (%)	Female N=17(%)	Male N=22 (%)
Hepatic	32 (82.05%)	12 (70.58%)	20 (90.90%)
Renal	10 (25.64%)	4 (23.52%)	6 (27.27%)
ARDS	21 (53.84%)	6 (35.29%)	15 (68.18%)
MODS	19 (48.71%)	4 (23.52%)	15 (68.18%)
Meningoencephalitis	4 (10.25%)	1 (5.88%)	3 (13.63%)
Sepsis	10 (25.64%)	3 (17.64%)	7 (31.81%)
Septic shock	6 (15.38%)	2 (11.76%)	4 (18.18%)

## Discussion

The present study has observed that scrub typhus can have a varied clinical presentation from only fever with or without eschar to fever with MODS [13]. A total of 39 cases of Scrub typhus confirmed by IgM ELISA positive out of which 56.42 % were male and 43.58% were females. The male preponderance may be associated with the local working culture of males being more involved in farming work. Maximum no. of the patients were farmers i.e. 30 (76.92%) and only 9 (23.08%) patients had other profession but indirectly they were also involved in farming works. Similar observations had also been observed in other Indian studies done by Sanjay v et al. [14]. In the present study, 87.17% of all our cases occurred in three months of peak rainy season (August, September, and October) which was similar to the study by Sanjay Vikrant et al [14] conducted in a western Himalayan state and only 13% cases occurred during rest of year which is statistically significant (p=.000). Most of the Scrub Typhus symptoms are nonspecific in nature including fever, breathlessness, myalgia, headache, vomiting etc and they usually don't vary among subjects of various different studies. In the present study, fever was the main symptom which was present in 100% of patients accompanied by headache, vomiting, cough, shortness of breath [14,15,16]. An eschar at the

Site of the bite is an important clue for diagnosis but there is considerable variation in the presence of eschar among various studies. In the present study the eschar was found in 7.69% of the patients which was very low in comparison to 41.7%, 46% from studies done by Dass et al at Meghalaya [12] and M. Vivekanandan et al [1] at Pondicherry, while most studies of the Oriental countries had eschar in 60-70% patients. Recent studies from northern India [17,18] and southern India [19,20,21] have also the similarly low level of prevalence of Eschar in their populations. The probable explanation for the less frequency of eschar in our area i.e. India specifically in Odisha is variation in cutaneous immunity as well as dark skin of the patients. Also, patients were unaware and ignore the presence of eschar leading to missing of that. Very rarely a detailed physical examination was done in search of an eschar [22] which also contributes to the low prevalence of eschar. The active search must be carried out to find the eschar at unusual locations, as this is a painless lesion. The rate of various complications is high in patients suffering from Scrub Typhus and the incidence is further high if there is a delay in diagnosis and treatment. In the present study, a large no. of patients has presented with complications probably due to delay in suspicion and diagnosis. Maximum no. of patients had Hepatic dysfunction with elevated liver enzymes i.e. 32(82.05%) which is similar to the studies conducted by Mahajan et al [6] and Jim et al [16]. A study conducted by Varghese GM et al showed that the incidence of ARDS was 43.5% which was similar to the current study with the incidence of 53.84% [23]. The incidence of Renal dysfunction was 25.64% in the present study which is comparable to that of Varghese et al with 13% and the result of the study by Sanjay Vikrant et al [14] with 35% but much lower than the result reported by Mahajan et al i.e.64.4% [18]. Out of 39 patients, about half (48.71%) were presented with MODS in the current study however the incidence of MODS in other studies like that conducted by Varghese GM et al was about 33.8% [23] which was quite comparable. In this study, altered sensorium was present in 10.25% patients with GCS below 15. In a study conducted by George M. Varghese et al [23] at Christian Medical College, Vellore has reported meningitis or meningoencephalitis in 19.2% which is comparable to result of the current study i.e. 10.25%. The mortality rate was considerably varied in different studies but the reasons for this have not been studied extensively. Overall, there is a decreasing tendency of case fatality rate due to

Scrub typhus as reports shown that scrub typhus outbreak in northern India had a mortality rate of 17.2%, in 2004 which subsequently decreased to 14% in 2006[24]. In the present study, the case fatality rate was nil.

## Conclusion

Scrub typhus is now a re-emerging infection in our country especially in Odisha with variable clinical manifestation from subclinical illness to severe illness making it difficult to differentiate from other infections. The clinical course also variable among different patients presenting with multiple organ system involvements, which can be serious enough to be fatal, unless diagnosed early and treated appropriately. Hence, to reduce the morbidity and mortality from Scrub typhus, all cases of acute febrile illness during this period i.e. rainy season should be evaluated for scrub typhus so that early treatment and other interventions can be possible.

## What this study adds to existing Knowledge

This study can provide an insight to the present knowledge of the clinicians about the Scrub typhus in the form of 1. The seasonal variation of occurrence and 2. About common complications which will help them for early suspicion and treatment of the patients suffering from Scrub typhus, thereby limiting the complication and mortality rates.

## Author's contribution

**Dr. Debananda Sahoo, Dr. Debasish Maikap, Dr. Lalatendu Mohanty, Dr. Shubhransu Patro, Dr. Sudhansu Sekhar Panda, Dr. Ambika Prasad Mohanty** have contributed equally in the writing and preparation of the manuscript.

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