An Analysis of Clinical Spectrum, Laboratory Profile, and Outcome of Scrub Typhus Cases in a Tertiary Care Hospital

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ABSTRACT:

BACKGROUND: Scrub typhus is a zoonotic illness caused by an obligate rickettsial bacteria \textit{Orientia tsutsugamushi}. It is a common cause of acute febrile illness in the tropics which is frequently ignored especially at times of viral outbreak. \textbf{AIM:} To analyse the clinical spectrum, laboratory profile and outcome of patients with scrub typhus. \textbf{METHODOLOGY:} This retrospective study was conducted in a tertiary care hospital based on medical records of those patients diagnosed with scrub typhus by clinical and laboratory parameters including serological tests(IgM ELISA) after ruling out other causes of acute febrile illnesses prevalent in study area.

\textbf{RESULTS:} Among study population (n=69), females were more commonly affected than males (59.4\%. versus 40.6\%). Fever was the most common presenting symptom. Eschar was noted in 73.9\% of subjects, most often in the external genitalia and groin. Most common laboratory abnormalities were thrombocytopenia (65.2\%) and elevated liver enzymes (84.1\%). Intensive care was required in 15.9\% of the cases and the mortality rate was 4.3\%. The most

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common complication observed was hepatitis (40.5%) followed by AKI (14.5%). CONCLUSION: This study highlights that Scrub typhus is one of the important differential diagnosis of fever in India, in which delayed treatment may be leading to high mortality. Presence of eschar helps in diagnosis but was not associated with severe disease in our study. Any patient presenting with acute febrile illness with thrombocytopenia and elevated liver enzymes should be evaluated for Scrub typhus in the current scenario of multiple outbreaks in various parts of India.

Key words: Acute febrile illness, zoonosis, scrub typhus, eschar, tropical fever, thrombocytopenia, elevated liver enzymes, AKI

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Introduction

Scrub typhus a febrile illness caused by obligate intracellular gram negative bacteria Orientia tsutsugamushi. It is transmitted to Homo sapiens by the bite an infected tromboculid mite - Leptotrombidium in its larval stage (called chigger).\(^1\) Scrub typhus is a major health crisis in South & Southeast Asia and also in the Pacific Rim with more than a million cases every year in these aforementioned regions. There are an estimated one billion people at high risk of contracting the disease. Several studies have shown Scrub typhus to be endemic to many states and union territories of India.\(^2\)\(^3\).

Though Scrub typhus was noted as early as 313.AD m large outbreaks of the disease was noted during world war II \(^4\). Earlier it was thought to be endemic in the “Tsutsugamushi triangle” that extends from northern Japan and far eastern Russia to northern Australia in the south and Pakistan in the west \(^5\). But reports from various parts of the world suggested that the disease is ubiquitous \(^6\).

The symptomatic manifestations of Scrub typhus include non-specific flu-like symptoms such as fever, hives, eschar at the bite site, headache, myalgia, cough, generalized lymphadenopathy, vomiting, and abdominal pain. Between 95% and 100% of confirmed cases were noted to have fever in several studies.\(^7\)

An eschar at the site of chigger feeding is a classic clinical feature of scrub typhus. It begins as a papule at the site of chigger feeding and then ulcerates and forms a black crust like a skin burn from a cigarette. When present, it occurs prior to the onset of fever and other symptoms.
Severe complications such as multiorgan failure occur in some cases. The severe multiorgan manifestations include jaundice, acute renal failure, pneumonitis, acute respiratory distress syndrome (ARDS), myocarditis, septic shock, meningoencephalitis, pericarditis, and disseminated intravascular coagulation (DIC). The lung is one of the main target organs for Orientia, leading to pulmonary complications of variable severity. Interstitial pneumonia may occur in severe cases. Meningitis and/or encephalitis can develop in severe illness, causing patients to become agitated, delirious or even have seizures.

The World Health Organization has dubbed scrub typhus one of the world’s most underdiagnosed/underreported diseases that often requires hospitalization, highlighting the necessity for a better understanding of the vectors, outbreaks, and pathogenesis associated with this potentially fatal organism that has been linked to human cases/outbreaks both within and beyond its previously recognized region of endemcity [8].

Though many studies have been reported all over India regarding outbreaks of scrub typhus in last two decades [1][9][10][11][12], this study is aimed at gaining better understanding of the existing knowledge on clinical spectrum, laboratory profile and outcome of Scrub typhus patients in our geographical area which helps in early diagnosis and prompt treatment.

Materials and Methodology:

Study Design:

The study was designed to be retrospective observational study and was carried out in the department of internal medicine and medical records section in a tertiary care center, who were admitted from February 2019 to January 2020.

Selection of Participants – Inclusion and Exclusion Criterion:

Only those patients of age ≥18yrs, with febrile illness having clinical and biochemical features suggestive of scrub typhus and tested positive for Scrub typhus IgM ELISA positive who are tested negative for other common febrile diseases such as dengue, malaria, typhoid and leptospirosis were included in the study.

The following patients are excluded from the study

- patients tested positive for other febrile illnesses in the preceding 3 months

• With overt cardiac/renal/hepatic dysfunction/malignancies/critically ill due to causes other than scrub typhus.
• Incomplete case records
• Negative serology for scrub typhus.

Data Collection:
After obtaining the institutional ethical committee clearance, the demographic details, history, examination findings including eschar site, investigations, treatment given, complications and outcome were noted for 69 patients who met inclusion and exclusion criteria. Complete hemogram, coagulation tests, liver function tests, renal function tests, serum electrolytes, blood and urine culture sensitivity, urine analysis and test to exclude malaria, dengue, leptospirosis and typhoid were done in all cases. The diagnosis of scrub typhus was based on detection of antibody against *Orientia tsutsugamushi* using a Rapid Elisa Kit. Other tests were done based on individual cases for fever workup and co morbidities. The complications such as ARDS, AKI, MODS, Myocarditis were defined as per standard reference book.

Statistical Analysis:
All collected data were processed and analyzed by using IBM SPSS version 20.0. Sample statistics i.e., mean, median and standard deviation were calculated for quantititative data. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student’s t-test. Test results were deemed significant at 95% confidence intervals P<0.05.

Results
A total of 82 cases were positive for Scrub typhus IgM ELISA during the study period and among these, 13 patients were excluded as per exclusion criteria, so there were 69 cases enrolled into the study. The mean age was 42.67 ± 11.35 years. 58% (n=40) of study population belonged to the age group of 31-50 years, followed by 24.6% (n=17) belonged to 51-75 years and 17.4% (n=12) belonged to below 30 years group.

The mean duration of hospital stay is 6.99 ± 3.60 days with a range of 3 to 28 days. The mean/median values of various study parameters are shown in table 1.
Females were more commonly affected than males (59.4% versus 40.6%). The most common presenting symptom is fever (88.4%) followed by respiratory symptoms (cough, breathlessness, etc.,) gastrointestinal symptoms (vomiting, nausea, diarrhoea, abdominal pain) and other symptoms (dysuria, oliguria, swelling, myalgia, etc.,). Diabetes was the most common co-morbidity (21.7%) followed by hypertension and hypothyroidism.

Eschar was noted in 73.9% patients (n=51). Lymphadenopathy was noted in 5.8% patients and hepatomegaly was noted in 2.9% of patients. The most common site of eschar noted were external genitalia and groin area followed by abdomen and axilla. Eschar was least common in back and lower limb. However Eschar in axilla was more common in females than males. The frequency distribution is shown in table 2.

The most common hematological abnormality among the study population was thrombocytopenia (65.2%) followed by anemia, leukocytosis and leucopenia. The median Platelet count was 128000 cells/cu.mm. Elevated liver enzymes were noted in 84.1% (n=58) and altered renal function was noted in 18.8% (n=13) (table 2). Few other interesting observations were hyponatremia (39.1%) and hypertriglyceridemia (59.4%) among study population. The electrocardiogram was normal in majority of study population (92.8%). ST segment and T wave changes were noted in 5.8% of patients (table 3).

The most common complication observed was hepatitis (40.5%) followed by acute kidney injury (14.5%). Other significant complications were Acute respiratory distress syndrome (10.1%), Septic shock (5.7%), MODS (4.3%), myocarditis (2.9%), meningoencephalitis (4.3%) (table 4). Intensive care management was required among 15.9% of patients. The mean duration of ICU stay was 1.12 ± 3.79 days. The case fatality rate in our study was 4.3%.

On comparing various parameters among survivors and non survivors, anemia, leukocytosis, thrombocytopenia, elevated urea, elevated creatinine and hyponatremia were found significantly higher in non survivors than survivors. Similarly AKI and ARDS were noted significantly higher among non survivors when compared with survivors. However, the presence of eschar did not differ significantly among the two groups. Table 5.

Discussion:

Scrub typhus is tropical disease endemic in Asia and is wide spread across South and Southeast Asia \[14\]. In India, the condition has been historically reported in the states of Assam, Himachal Pradesh, West Bengal, Kerala, Karnataka and Tamil Nadu. In recent times, there has been a reemergence of scrub typhus in India after few years of
dormancy. Over the past twenty years, rapid urbanization leading to population displacement towards urban centers, rise in antimicrobial resistance caused by indiscriminate antibiotic usage and climate change due to global warming might have played a critical role in the increased number of scrub typhus in India. Unplanned urbanization coupled with mass influx of population places a massive pressure on sanitization systems, resulting in accumulation of garbage and increased population of rats which act as a reservoir of typhus infection. Similar trends have been observed in newer urban areas of South Korea.

In this scenario, analyzing the clinical spectrum of scrub typhus along with laboratory profiles of the patients with this condition and understanding how it is associated with the treatment outcome in a metropolis like Chennai with high population density will be invaluable in making future plans to tackle the reemergence of the disease in India.

The mean age was 42.67 ± 11.35 years with maximum number of patients in 31 to 50 years group. Varghese et al also observed similar mean age. Philomena et al observed that 48.5% of cases belonged to age group 18 - 30 years followed by 31 to 40 years (23%). Singh et al also observed that majority of cases in 21 to 50 years group (68.1%). Pathania et al observed that 64.82% belonged to 20-40 years group. There was a female preponderance (59.4% versus 40.6%) in our study similar to that of Varghese et al, Philomena et al, Pathania et al. This shows that adult of age less than 50 years are more commonly affected and females are more commonly affected than males.

Fever is the most common presenting symptom in most of other studies. Eschar was noted in 73.9% patients and the most common site of eschar noted were external genitalia and groin area followed by abdomen and axilla. The percentage of eschar significantly varies in studies done from various parts of India from 0 to 45%. This may be due to variability in dark skin, dressing styles, clinician error and difference in subtype of causative organism. The site of eschar is very similar to that other studies (Jamil, Vivekandan, Rajendra Prasad, Pathania, Philomena). The eschar reported in few other Asian studies are higher than Indian studies which may be explained by darker skin and altered strains of causative organisms.

Thrombocytopenia was observed in 65.2% of cases. Thrombocytopenia was noted in 79% of cases by Varghese et al, 56% by Philomena et al and 63.3% by Sivarajan et al similar to our study, but other Indian studies have
reported lesser incidence of thrombocytopenia. Mildly elevated liver enzymes were noted in 84.1% and it is the most common laboratory abnormality noted. This finding is similar to many other studies. Varghese et al. (n = 50), a combination of elevated transaminases, thrombocytopenia and leucocytosis displayed 80% specificity and 80% positive predictive value for scrub typhus diagnosis. An interesting observation is hyponatremia noted in 39.1% of cases. Few other Indian studies have reported that hyponatremia could be an earlier pointer in resource limited setting. This finding may need further investigation.

Most of our patients were treated with doxycycline 100mg po bd for 14 days, whereas azithromycin 500mg od was initiated in patients who were intolerant to doxycycline or was contraindicated. IV antibiotics were preferred in patients requiring intensive care. Patients were also subjected to hemodialysis and mechanical ventilation when indicated.

Intensive care management was required among 15.9% of patients. Hepatitis (40.5%) was most common complication followed by AKI (14.5%), ARDS (10.1%), Septic shock (5.7%), MODS (4.3%) and Meningoencephalitis (4.3%). This is very similar to that of study by Varghese et al, where Hepatitis (34%) was most common followed by ARDS (33.7%) and AKI (18%). Vivekanda et al also reported Hepatitis as most common complication followed by meningitis, AKI and ARDS. The presence of shock and CNS manifestations were comparatively lesser in our study.

The case fatality rate in our study was 4.3%. Recent studies from various parts of India are reporting mortality rates from 1 to 10% which may be attributed to early diagnosis and prompt treatment by clinicians due to increased awareness. Varghese et al noted 9% fatality rate and it was also pointed the fatality rate is decreasing compared to their previous study. The presence of AKI and ARDS were noted to be significantly higher among non survivors when compared with survivors.

The limitations of this study are usage of serological tests for diagnosis rather than immunochromatographic method assays which could have missed the diagnosis when tested early.

**Conclusion**

This study highlights on the various clinical manifestation and laboratory parameters of Scrub typhus. That eschar occurrence was found to be relatively common in scrub typhus, and hidden sites of eschar must be kept in mind and
looked for on examining any patient presenting with acute febrile illness. Delayed diagnosis can lead to a variety of complications and need for intensive care. Considering the increased number of cases reported in India due to its reemergence, there is a need for increased awareness amongst physicians.

References


