

# SCRUB TYPHUS IN NORTH KERALA

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## Medicine

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### Abstract:

**Background and Objectives :** Scrub typhus is an emerging epidemic in north Kerala. A retrospective observational study was conducted to describe the epidemiological, clinical and laboratory manifestations of Scrub Typhus.

**Materials and methods:** Data were retrieved from inpatient records of patients who were admitted with scrub typhus in the Medicine wards in the year 2012.

**Results:** Among 26 cases admitted in the year 2012, 15 were males. Mean age was 38. Patients were from Kozhikode, Wayanad and Malappuram districts. Incidence peaked between December and March. Mean duration of fever was 10 days. Headache and body ache were the most common associated symptoms seen in 88% and 77% cases. Eschar was seen in 3 cases only. Derangement in vital signs disproportionate to rise in temperature indicated myocarditis and ARDS. Leukocytosis was seen in 11 cases and ESR was elevated in most patients. Weil Felix test was positive in 68%. Most of the patients had modest elevation of liver enzymes. Clinical presentation mimicked that of enteric fever, Malaria, Leptospirosis, viral fever, malaria and atypical pneumonia in many patients. Thrombocytopenia was the most common complication. ARDS was the fatal complication and was seen in 2 cases.

**Conclusions:** Scrub typhus should be included in the differential diagnosis of patients with acute undifferentiated febrile illness including those with multi system involvement. Thorough search for eschar has to be done in all cases. Rapid response to doxycycline is characteristic. Enteric fever, leptospirosis, malaria and non viral illnesses can be excluded using clinical methods and simple laboratory tests.

**Keyword:** Scrub typhus, Kerala, Epidemiology

### Introduction

Scrub typhus is an acute febrile illness caused by *Orientia Tsutsugamushi* and transmitted by mites. In Kerala, it is emerging as an important cause of acute febrile illness which closely mimics other common febrile illnesses like leptospirosis, typhoid, *Falciparum* malaria and dengue fever. Awareness of the clinical profile and of the changes in common laboratory parameters help in early differentiation between these disorders. Early initiation of treatment with doxycycline gives complete cure in scrub typhus. Several cases of scrub typhus have been confirmed in the

Government Medical college, Kozhikode in 2011 and 2012. This study attempts to understand the clinico epidemiological profile of scrub typhus in the population of north Kerala to help the clinicians in the periphery to identify scrub typhus early in the course and manage them effectively.

### Aims of the study

1) To describe the diverse clinico epidemiological and laboratory manifestations of scrub typhus diagnosed in Government medical college Kozhikode in the year 2012.

2) To take an account of the complications and mortality and the possible causes associated with them in scrub typhus.

criteria as the test has low sensitivity and becomes positive only by second week (5,6). Other specific tests of scrub typhus were not done due to financial constraints.

## Materials and methods

A retrospective observational study was conducted. All the adult cases (age more than 12) admitted with scrub typhus in the Medicine wards of Government medical college Kozhikode in the year 2012 were included. Data was retrieved from the case records regarding epidemiological parameters, history and physical examination findings, investigation details, course in the hospital, treatment and the outcomes.

Diagnosis of scrub typhus was made in the presence of any three of the following features in an appropriate epidemiological setting like working in bushy areas or shrubs prior to onset of fever.

Clinical features suggestive of scrub typhus with or without the presence of typical eschar

Prompt response to doxycycline

Positive Weil Felix test with titer more than 1:160

Exclusion of other common differential diagnoses

Positive Weil Felix test is not considered as an essential

## Results

Twenty six patients were diagnosed to have scrub typhus during the study period of one year. Their age ranged from 14 to 67 years with a mean age of 38. Maximum number of patients was in the age group of 30-50 years. There were 15 females and 11 males. All the patients were from the rural areas of Kozhikode(12), Wayanad (9) and Malappuram(5) districts. Maximum number of cases were seen during the cooler months (between December & March).

## Clinical features

All the patients had fever with a mean duration of 10 days (Table 1). Other common symptoms were headache, body ache, vomiting and cough (Table 2). Headache was seen in 88% of the cases. Gastrointestinal symptoms were also present in many patients. The typical Eschar was noted in three patients only. Small Lymph nodes were palpable in four patients, in the cervical and axillary groups. Hepatomegaly and splenomegaly were the other clinical signs noted. A few patients had disproportionate tachycardia, tachypnea and hypotension (Table 2)

**Table 1- Duration of Fever**

Duration of fever	Number of patients
1-7	4
7-14	16
>14	6

**Table 2: Symptoms and Signs**

Symptoms	n (=26)	Percentage	Clinical signs	n(=26)	Percentage
Headache	23	88	Pedal Edema	1	3.8
Bodyache	19	73	Jaundice	1	3.8
Arthralgia	2	7.7	Eschar	3	11.5
Cough	9	34.6	Rash	2	7.7
Breathlessness	6	23	Tachycardia	5	19
Altered sensorium	4	15	Tachypnea	3	11.5
Nausea and vomiting	15	58	Hypotension	4	15
Abdominal pain	2	7.7	Lymphadenopathy	4	15
Constipation	3	11.5	Hepatomegaly	4	15
Diarrhea	2	7.7	Splenomegaly	5	19

Leukocytosis was noted in 42% of the cases whereas ESR was found to be elevated in most cases (Table 3). SGOT and / or SGPT were modestly elevated in 80% cases (Table 4). Serum bilirubin level was raised in nine patients (30%). Four patients had altered renal function tests, out of whom

two had a definite history noted regarding NSAID intake. Chest roentgenogram showed diffuse infiltration in two patients. CSF abnormalities were noted in three patients (mild to moderate increase in lymphocyte count and protein). Weil Felix test was positive in 17 patients (68%).

**Table 3 : Laboratory parameters in Scrub Typhus**

Total WBC count	Number (n=26)	Percentage	ESR	n=26	Percentage
<4000	2	7.7	25-50	5	19
4000-11000	13	50.3	50-75	7	27
>11000	11	42	75-100	6	23
			>100	4	15

**Table 4: Liver enzymes in Scrub Typhus**

SGPT			SGOT	
Values	n=26	Percentage	n=26	Percentage
<40	5	19	4	15
40-100	11	42	5	19
100-200	5	19	2	7.7
200-300	2	7.7	2	7.7
>300	2	7.7		

Initial diagnosis made at the time of admission (Table 5)

In spite of the high index of suspicion prevailing among the doctors in our institution, Scrub typhus was suspected at the time of admission in only 50% of the cases. In the rest of the cases, the clinical features at the time of admission were more suggestive of alternate diagnoses like enteric fever, non specific viral illness, malaria and atypical pneumonia. In these cases, subsequent evaluation after admission led to the final diagnosis of scrub typhus.

**Table 5**

Initial diagnosis	n=26	Percentage
Scrub typhus	13	50
Enteric fever	7	27
Viral fever	3	11.5
Malaria	1	3.8
Atypical pneumonia	1	3.8

#### Complications ( Table 6)

Thrombocytopenia was the most common complication.

Meningo encephalitis was seen in five patients and all were self limiting. Myocarditis and acute kidney injury were noted in four patients each. ARDS was seen in two patients and was fatal in both cases.

**Table 6**

Complications	n=26	Percentage
Meningo encephalitis	5	19
Myocarditis	4	15
Acute kidney injury	4	15
ARDS	2	7.7
Thrombocytopenia	11	42

#### Mortality

Two patients died of scrub typhus complicated by ARDS. Details of both cases is given in table 7.

**Table 7**

Age	Sex	Duration of fever	No: of Days hospitalised	Complications	Hypotension	WBC count	ESR	Creatinine	Chest X-ray features of ARDS
34	F	7days	3 days	Myocarditis, ARDS	Yes	8900	60	0.5	Yes
24	F	7days	8 days	ARDS	Yes	8300	50	2.7	Yes

## Discussion

There has been several reports of scrub typhus from various parts of the country recently(1-4). It presents in most cases as a non specific acute febrile syndrome affecting previously healthy manual labourers. A delay in diagnosis can be fatal. A high index of suspicion and awareness of the epidemiological setting and awareness of its varied manifestation is very important for early diagnosis. Clinician should not depend too much on the serological diagnosis which will be negative in the early phases and could be false positive sometimes (10).

Weil Felix test is a cheap and widely available test used for confirming the clinical suspicion of scrub typhus. This test is based on the detection of antibodies to various Proteus species which contain antigens with cross reacting epitopes to antigens from members of the genus Rickettsia. Positive test with Ox-K strain of Proteus mirabilis is suggestive of scrub typhus. In a study conducted at Christian Medical College Vellore, it was found that the sensitivity of Weil Felix Ox-K was 30% at a titre of 1:80, and the specificity and positive predictive values were close to 100%(7). Weil-Felix test results may be negative during the early stages of the disease because agglutinating antibodies are detectable only during the second week of illness(8,9). False positive reactions can occur with sera from patients with urinary tract infections due to proteus organisms, leptospirosis, and relapsing fevers(10). The specific immunological tests for unequivocal diagnosis are immunofluorescent antibody test (IFA), immunoperoxidase test (IIP), enzyme immunoassays and PCR amplification of Orientia from eschar and blood. These tests are not necessary except in research settings.

Duration of fever was more than ten days in half of our cases. That helps in distinguishing it from leptospirosis and common viral infections like dengue fever. Apart from the duration of fever, relatively high WBC count and elevated ESR if present helps in ruling out viral infections. Leptospirosis, which is endemic in Kerala, has

similar features in the early stages and similar course and complications except for the duration of fever which is short in Leptospirosis. The absence of muscle tenderness, conjunctival congestion or jaundice also helps in this context. There is a seasonal variation in that Leptospirosis is seen more commonly in rainy seasons, that too soon after the rain (June to September) where as scrub typhus is more common in December to April but both can occur in any season in the appropriate epidemiological setting. The history of exposure to contaminated soil or water is easily available in Leptospirosis. Besides, doxycycline can be used effectively in both conditions and therefore if there is a suspicion of any of these, early treatment with doxycycline saves the patients. Enteric fever has a closely mimicking clinical profile, but there need be no hurry usually in initiating its treatment for it. In patients with enteric fever, there is usually a history of travel and consuming food or water in unhygienic surroundings. Whereas in scrub typhus there is a history of trespass into shrub or forest cleared vegetations. The rapid response to doxycycline within 1-3 days also favour scrub typhus. Malaria should also be considered depending on the epidemiological setting.

Eschar at the site of attachment of mite is the characteristic clinical sign of scrub typhus. It is a black necrotic area found in areas where the skin is thin and the clothing is tight where the mites are stopped and rubbed against the skin, usually in the axilla or groin. Patients are generally unaware of eschar as it causes no discomfort. Patients have to be examined thoroughly removing all cloths to detect it. Even then eschar is not seen in most of the cases. So the clinician cannot depend on the presence of eschar to make the diagnosis of scrub typhus.

Thrombocytopenia was the most common complication and the lowest count was 26000/cmm. There were no bleeding manifestations and count recovered within 3-4 days. Prominent headache and drowsiness indicated meningoencephalitis. CSF study showed lymphocytic pleocytosis in three cases and normal results in two cases

of suspected meningoencephalitis. It was self-limiting in all the cases. Acute kidney injury was seen in four patients out of which two had definite history of NSAID intake for body ache, possibly the other two would also have received NSAID during fever. Hence the use of NSAID for the myalgia associated with febrile illnesses of any cause has to be curtailed. Myocarditis was seen in four patients, all of whom had disproportionate tachycardia and two of whom had hypotension requiring inotropic support. All patients with myocarditis recovered except one who had associated ARDS. The derangement in vital signs disproportionate to the degree of rise in temperature may help as indicators of serious complications like myocarditis and ARDS. Breathlessness associated with cough portended ARDS, which showed diffuse infiltrates in Chest X-ray. Both the patients who had ARDS expired.

Doxycycline was the antibiotic used in all cases. Response to doxycycline was seen within 1-3 days. The response to treatment with Doxycycline was so dramatic that it can even be used as a therapeutic test. All the patients tolerated doxycycline well.

## Conclusions

The incidence of scrub typhus is increasing in rural areas of Kerala. It should be considered in the differential diagnosis of patients with acute febrile illnesses, including those with thrombocytopenia, renal impairment, elevated liver enzymes, altered sensorium, myocarditis, or ARDS. A high index of clinical suspicion, awareness of the epidemiological setting, thorough history and probing search for an eschar, particularly in the hidden areas is very useful for diagnosis. However, the eschar may not be seen in the majority of the cases. Weil Felix test is a cheap alternative to the more specific tests. Empirical therapy with doxycycline is life saving when clinical suspicion is high, even if Weil Felix test is negative and eschar is not present.

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