

## ORIGINAL ARTICLE

# Early Clinical Suspicion and Early Use of Doxycycline Reduces Scrub Typhus Associated Complications

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## Abstract

**Background:** Scrub typhus has emerged as an important cause of febrile illness in this Himalayan region of the country. However, it is under considered in the differential diagnoses of febrile illnesses and is not treated and thus, patients often land up with complications in this tertiary care hospital.

**Methodology:** It was a retrospective observational study done in department of Medicine from August 2013 to October 2013. All the patients more than or equal to 18 yrs of age admitted during this period with scrub typhus were analysed and their outcome followed. S. ELISA was used to detect scrub typhus.

**Results:** Total of 106 patients were observed out of which only 10 patients had received anti scrub antibiotics (doxycycline or azithromycin) prior to admission. Seven patients died (6.6%) and none had received anti scrub antibiotics prior to hospitalisation and presented late with average duration of illness of 9.2 days and had more severe form of complications at presentation. Those patients who had received prior anti scrub treatment had fewer and mild complications and none died among that group.

**Conclusion:** Doxycycline or azithromycin (pregnancy or in child <8 years) should be included in the initial empirical antimicrobial therapy in febrile patients during tick season to treat scrub typhus. The goal is to begin anti-scrub therapy early to reduce the morbidity and mortality associated with this illness.

## Introduction

Recently scrub typhus has emerged as an important cause of febrile illness in this Himalayan region of the country. However, it is under considered in the differential diagnoses of febrile illnesses and is not treated and thus, patients often land up with complications in this tertiary care hospital. It is a mite borne rickettsial disease caused by *Orientia tsutsugamushi* leading to widespread vasculitis and consequently organ dysfunction.<sup>1,2</sup> Its early clinical manifestations are nonspecific and are characterized by fever, chills, headache, and myalgia. These are easily overlooked and consequently patients often present with severe complications which otherwise can be prevented with early clinical diagnosis and treatment. Severe complications of scrub typhus reported; includes interstitial pneumonia, acute renal failure, meningoencephalitis, gastrointestinal bleeding, and multiple

organ failures. Patients often die because of these complications.<sup>3,4</sup> During the pre-antibiotic era, the overall mortality was 50%. As the effective antibiotics came, the mortality and morbidity has decreased. For various reasons effective treatment is often delayed, prominent of which is failure to suspect scrub typhus as a cause of febrile illness by the primary care physician. Consequently, patients presents with complications. Therefore, this study was conducted to assess the failure of the primary care doctor to consider scrub typhus as a cause of pyrexia and delay in appropriate treatment as a factor for increased morbidity and mortality among patients with scrub typhus.

## Methodology

It was a retrospective observational study done in department of Medicine from August 2013 to October 2013. All the patients more than or equal to 18 yrs of age admitted during this period with scrub typhus were analysed and their outcome followed. Scrub typhus was defined as the patient presenting with fever, myalgias, headache with or without eschar with positive IgM titre against *O. tsutsugamushi* done by ELISA method. Other causes of acute febrile illness were excluded with appropriate investigations. History and relevant general physical and systemic examination were recorded and complete haemogram, biochemical parameters and relevant radiological investigations were conducted. Complications documented and data was analysed.

## Results and Discussion

We analysed total of 106 patients; out of which 64 were females (60.37%) and 42 (39.62%) were males. Maximum number of patients; 56 patients (52.83%) were from Shimla district followed by 20 patients (18.86%) from Mandi and 12 patients (11.3%) from Bilaspur. The epidemiological and clinical observations shown in Table 1.

Mean age of presentation was  $39.68 \pm 3.12$  yrs for females and  $42.78 \pm 4.23$  yrs for males. Maximum number of patients (37.73%) presented in the age 40 to 60yrs; followed by age group 20-40 (36.79%). 60.37% patients were female in our study as females are mostly engaged in farming and other outdoor activities in this tiny hilly state and hence exposed to mites causing scrub typhus. Our demographic profile is similar to studies conducted in other

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**Table 1: Profile of patients**

Total	Total (%)	males	Females
Number of patients (n)	106	42	64
Areas of presentation (n)			
Shimla	56 (52.8)	25	31
Solan	8 (7.5)	5	3
Mandi	20 (18.9)	4	16
Kullu	5 (4.7)	1	4
Bilaspur	12 (11.3)	5	7
Others	5 (4.7)	2	3
Age of presentation (yrs.)			
<20 yrs	14 (13.2)	3	11
20-40 yrs	39 (36.8)	8	31
40-60 yrs	40 (37.7)	24	16
60-80 yrs	12 (11.3)	6	6
>80 yrs	1 (0.9)	1	0
Symptoms (n)			
Fever < 7 days	78 (73.6)	27	51
>7 days	28 (26.4)	15	13
Altered sensorium	45 (42.4)	20	25
Diarrhoea	16 (15.1)	5	11
Shortness of breath	35 (33.0)	12	23
Pain abdomen	18 (17)	7	11
Jaundice	38 (35.8)	17	21
Headache	12 (11.3)	3	9
Seizures	3 (2.8)	0	3
Duration of illness (mean days)	6.2± 2.3	7.1± 1.5	
Treatment			
Some form (total)	62 (58.5)	21	41
Anti scrub antibiotics	10 (9.4)	3	7
Other than anti scrub antibiotics	52 (49)	18	34
Not received treatment	44 (41.5)	21	23
Outcome			
Died	7 (6.6)	2	5
Improved	99 (93.4)	40	59
Complications			
Liver dysfunction	67 (63.2)	23	44
Renal dysfunction	48 (45.3)	17	31
Meningitis/meningoencephalitis	23 (21.7)	8	15
ARDS/ALI	32 (30.1)	11	21
Shock	14 (13.2)	5	9

parts of country.<sup>5,7,9</sup> Mean duration of illness was 6.2 ± 2.3 days among females and 7.1 ± 1.5 days among males. This is in accordance with other studies.<sup>5-9</sup> All patients presented with fever as chief complaint followed by altered sensorium in 45 (42.45%), jaundice in 38 (35.84%), shortness of breath in 35 (33.01%), pain abdomen in 18 (16.98%), diarrhoea in 16 (15.09%), headache in 12 (11.32%) and seizures in 3 (2.83%) patients. This profile of presentation is similar to that observed in other studies.<sup>7,8</sup> Total 62 patients (58.49%) had received some form of treatment prior to the admission in this institution and out of these only 10 patients

**Table 2: Outcome and complications in patients receiving prior doxycycline vs no treatment**

	Total	Received doxycycline	No treatment or no doxycycline
Total	106	10 (9.4%)	96 (90.6%)
Mortality	7	0 (0%)	7 (6.6%)
Complications			
Liver dysfunction	67	3 (2.8%)	64 (60.4%)
Renal dysfunction	48	4 (3.7%)	44 (41.5%)
Meningitis	23	0 (0%)	23 (21.69%)
ARDS/ALI	32	0 (0%)	32 (30.1%)
Shock	14	0 (0%)	14 (13.2%)

had received anti scrub antibiotics (doxycycline or azithromycin) and rest 52 patients received some non-specific therapy in the form of cephalosporin, anti-pyretic and multi-vitamins. 44 patients did not receive any treatment before presentation at this institution. Out of the total patients; seven died (6.6%) and rest all (93.39%) improved with the in hospital treatment. This mortality rate is similar (7.8%) to studies conducted by Varghese et al,<sup>9</sup> less (12.2%) that that found by Kim et al.<sup>6</sup> Complications rates observed were also high with 67 patients (63.2%) developing hepatic dysfunction with raised bilirubin and aminotransferase, 48 patients (45.28%) developing renal dysfunction and 14 patients requiring renal support, 23 patients (21.69%) having CNS manifestations, 14 patients (13.2%) having shock and 32 patients (30.1%) having either acute respiratory distress syndrome or acute lung injury. These rates of complications were in accordance with other studies.<sup>10,11</sup> Seven patients who died none had received anti scrub antibiotics prior to hospitalisation and presented late with average duration of illness of 9.2 days and had more severe form of complications at presentation. Those patients who had received prior anti scrub treatment had fewer and mild complications (hepatic and renal dysfunction) and none died among that group (Table 2). Patients who survived despite not receiving anti scrub treatment before hospitalisation presented early with average duration of illness of 6.8 days and had only mild form of renal, hepatic, nervous system and lung dysfunction (ALI).

### Conclusion

Scrub typhus is a serious febrile disease in this part of the country

with nonspecific symptoms but high mortality and complication rates. Failure to receive doxycycline in early course of disease leads to prolonged disease course, increased complications and mortality and increased expenditure on treatment. Because of unavailability of laboratory facilities in the peripheral health institutions, the diagnosis of scrub typhus should be based on high index of clinical suspicion and careful clinical examination; especially during the rainy season of the year when scrub typhus is rampant. Doxycycline or azithromycin (pregnancy or in child <8 years) should be included in the initial empirical antimicrobial therapy in febrile patients during tick season to treat scrub typhus. The goal is to begin anti-scrub therapy early to reduce the morbidity and mortality associated with this illness. Health education is also of paramount importance to spread awareness among health care providers and public not only about how to prevent and control scrub typhus but also about early use of doxycycline in febrile patients during scrub season to reduce the complications.

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