

# Clinical Manifestation and Complications of Scrub Typhus Cases: A Hospital-based Observational Study from Rural Part of West Bengal

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## ABSTRACT

**Introduction:** Scrub typhus is very common re-emerging Rickettsia infection in India and many other South East Asian countries. The unplanned urbanization, deforestation and easy transportation leads to changes of place of occurrence of scrub typhus from hilly and forest terrains to plan land with different clinical manifestation. **Aim:** This study was conducted to identify the regional characteristic of clinical sign, symptom and treatment outcome of scrub typhus patients admitted in a tertiary level hospital of Murshidabad district of West Bengal. **Methods:** An observational cross sectional study was conducted among 82 hospitalized scrub typhus patients during September, 2019 to March, 2020. Patients were selected by purposive sampling procedure. Data were analyzed in descriptive statistic. **Results:** All study participants presented with acute febrile illness with other symptoms like headache, cough, dyspnea, nausea, generalized weakness, abdominal pain and myalgia. On examination, patients had hepatosplenomegaly (21%), lymphadenopathy (7%), pedal edema (14%), Icterus (12%) and eschar (4%). On investigation, elevated ALT (37%), elevated AST (36%), Low platelet count (25%), low Hb% (52%), elevated WBC count (37%) levels were the most common findings. Interestingly few patients diagnosed with co-morbid infections eg: enteric fever (12%), Urinary tract infection (12%), respiratory tract infection (27%), dengue fever (5%) and malaria (2%). Low mortality rate (4%) was observed due to tertiary level health care services and increased awareness among local medical fraternities on scrub typhus apart from lower virulence or indigenous resistance as host or environment factor. **Conclusion:** Scrub typhus is an important zoonotic disease of variable presentation with low fatality if diagnosed and treated early. It is necessary to include scrub typhus serology test as routine blood test for all acute febrile illness patients for this area.

**Key words:** Scrub typhus, Complications, Observational Study, Murshidabad.

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## History

- Submission Date: 29-06-2020
- Revised Date: 25-08-2020
- Accepted Date: 30-10-2020

DOI : 10.5530/ijmedph.2020.4.39

Article Available online

<http://www.ijmedph.org/v10/i4>

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## INTRODUCTION

Scrub typhus is a zoonotic infectious disease caused by an intracellular parasite *Orientia tsutsugamushi*, a Gram-negative proteobacterium of family Rickettsiaceae, first identified in Japan in 1899.<sup>1</sup> Humans are accidental host after exposed with chigger mite infested rural or semi urban fields particularly crop fields. It was considered a deadly disease in pre antibiotics era where as they have been brought under control in most of developed Asian nations.

In India, scrub typhus broke out in an epidemic form in Assam and West Bengal during the Second World War. Gradually, the disease became prevalent in many parts of India. In recent time, scrub typhus has re-emerged to become the major cause of Acute Febrile illness (AFI) in many parts of India (Shivalik ranges from Kashmir to Assam, Eastern and Western Ghats and the Vindhya and Satpura ranges in the central part of India)

with myriad clinical presentation.<sup>2</sup> Recently Bihar witness a massive scrub typhus outbreak as most common cause of Acute Encephalytic Syndrome on 2018.<sup>3</sup> Himachal Pradesh, Sikkim and Darjeeling (West Bengal) also witnessed scrub typhus outbreak during 2003–2004 and 2007.<sup>2</sup> In a study published from Rajasthan, authors noted scrub typhus as an emergent cause of acute renal failure.<sup>4</sup>

In this study area, we witnessed surge of dengue fever which is the most common cause of AFI in couple of decades. Further we also experienced sudden increases of scrub typhus cases which may mimic with dengue fever and other acute febrile illnesses in this area. However, officially there is no declaration from state government on this sudden increase of scrub typhus cases as 'scrub typhus outbreak' of this area. Present study have been carried out to document clinical features and complications including mortality and co-morbid

**Cite this article :** Sarkar K, Acharyya A, Ghosh S, Ghosh M, Bhattacharya A, Ghosh K. Clinical Manifestation and Complications of Scrub Typhus Cases: A Hospital-based Observational Study from Rural Part of West Bengal. Int J Med Public Health. 2020;10(4):180-3.

disorders among diagnosed scrub typhus patients who were admitted in Monmohini Multi-specialty Hospital, Murshidabad hospital during September 2019 to February 2020. This study may provide information regarding regional variability of presenting clinical pattern of scrub typhus patients in this area.

## Methodology

A cross sectional descriptive observational study was conducted among admitted scrub typhus patients at Monmohini Multi-specialty Hospital, Murshidabad during September 2019 to March 2020. All clinically suspected cases with acute febrile illness were investigated for malaria, dengue, scrub typhus, HIV-AIDS, HCV, Urinary tract infection (UTI), respiratory tract infection (LRTI/URTI), Pulmonary tuberculosis (PTB) and leptospirosis on admission. After establishing the cause of fever, total 82 scrub typhus IgM serology positive patients were included in this study. The related socio-demographic data were collected during admission procedure. The data related with clinical findings, laboratory reports, vital signs, treatment outcome of each patient were collected from patient bed head ticket from record section of the hospital.

Basic laboratory evaluation included complete blood count (CBC), peripheral blood smear, liver and renal function tests and chest X-ray were carried out of each patients. Other tests such as cerebrospinal fluid analysis, magnetic resonance imaging brain were performed as indicated. A diagnosis of scrub typhus was confirmed when a patient with an AFI had a positive serology for scrub typhus.<sup>4</sup> Patients were included by purposive sampling procedure.

All patients were treated with empirical antibiotic (Injection Ceftriaxone) and symptomatic treatment medicines. After confirmation of diagnosis, the doxycycline was administered with other antibiotics as indicated to deal with other co-morbidities.

Data were analyzed by SPSS (IBM) software. Only descriptive statistic was performed in data analysis. The permission of the study was obtained from Institution Ethical Review Committee and informed consent was obtained from the patients.

## RESULTS

A total 82 scrub typhus patients were included in this study. Majority of patients were literate (98%), female (54%) and belongs to 21-49 age group (55%). Regarding occupation, 34%, 23%, 18% subjects were housewife, student and serviceman respectively (Table 1).

The most common clinical presentation on admission were fever (100%), generalized weakness (54%), abdominal pain (39%), headache (37%) and nausea (48%). Other notified clinical symptoms were breathlessness, cough, altered sensorium, myalgia, upper lid oedema, rashes, hemoptysis and decreased Urine output. (Table 2) The common clinical sign were hepatosplenomgaly (21%), pedal oedema (14%), Icterus (12%) and hypotension /shock (11%) etc. Eschar (Figure 1) and lymphadenopathy were found among 4% and 7% cases respectively (Table 3).

Among all patients, anemia (Hb<11gm/dl), WBC count < 4000/cumm, WBC count >11000/cumm, plural effusion and elevated ALT found among 52%, 05%, 37%, 20% and 37% persons respectively. Interestingly few patients diagnosed with co-morbid infections eg: enteric fever (12%), Urinary tract infection (12%), respiratory tract infection (27%), dengue fever (5%) and malaria (2%). No any patient found with co-morbid infection with HIV-AIDS, hepatitis, HCV and leptospirosis infections. 21 (25%) patient's platelet count dropped below 1 lakh/cumm (Table 4).

The maximum patients stayed in the hospital for treatment was 1-4 days (56%) and only 29% patients required ICU treatment. Only twelve (15%) patients required ventilation support. 3 (4%) patients' required hemo-

**Table 1: Distribution of socio-demographic variables of scrub typhus patients (n: 82)**

Variables	n (%)
<b>Age (years) Mean : 38.35</b>	
≤20 years	15 (18)
21-49 years	45(55)
50≥ years	22(27)
<b>Gender</b>	
Male	38 (46)
Female	44 (54)
<b>Literacy</b>	
Literate	80 (98)
Illiterate	02 (2)
<b>Occupation</b>	
Student	19 (23)
House wife	28 (34)
Service	15 (18)
Business	12 (14)
Retired	08(11)

**Table 2: Distribution of clinical symptoms of scrub typhus patients on admission (n: 82)**

Symptoms	n	Percentage
Fever	82	100
Breathlessness	25	30
Decreased Urine output	04	05
Altered sensorium	13	16
Rash	04	05
Nausea	40	48
Myalgia	13	16
Cough	23	29
Headache	31	37
Haemoptysis	03	04
Generalized weakness	44	54
Abdominal pain	33	39
Upper lid oedema	07	09

**Table 3: Distribution of clinical signs of scrub typhus patients on admission (n: 82)**

Signs	n	Percentage
Eschar	03	04
Icterus	10	12
Lymphadenopathy	06	07
Pedal oedema	12	14
Hypotension/shock	09	11
Hepatospleomegaly	18	21

**Table 5: Distribution of treatment and treatment outcome related variables of scrub typhus patients (n: 82)**

Variables	n	Percentage
<b>Duration of stay</b>		
< 5 days	44	54
5-10 days	35	43
>10 days	03	4
<b>Duration of ICU stay</b>		
1-4 days	15	18
5-10 days	08	11
>10 days	00	00
<b>Hemo-dialysis</b>		
Yes	03	4
No	79	96
<b>Mechanical ventilation required</b>		
Yes	12	16
No	69	84
<b>Type of mechanical ventilation</b>		
Non-invasive	08	11
Invasive	03	04
Both	01	02
<b>Medicine used</b>		
Doxycycline Only	25	31
Doxycycline +Ceftriaxone	13	16
Doxycycline + Azithromycin	13	16
Doxycycline + Other	31	37
<b>Mortality</b>	03	04

**Table 4: Distribution of report of investigations of scrub typhus patients (n: 82)**

Variables	n	Percentage
Hb<11gm/dl	42	52
WBC < 4000/cumm	04	05
WBC>11000/cumm	31	37
Platelet count <1 lak/cumm	21	25
Increased bilirubin	12	14
Increased urea/creatinine	08	10
Elevated transaminase levels	19	23
Elevated AST	29	36
Elevated ALT	31	37
Typhoid IgM positive	10	12
HCV IgM positive	00	00
HbsAG	00	00
HIV positive	00	00
Malaria	01	02
Dengue	04	05
LRTI/URTI	22	27
UTI	10	12
Plural Effusion	16	20

**Figure 1:** Eschar on the body surface of scrub typhus patient.

dialysis support. The observed mortality was 3 (4%). ARDS developed among two patients. Two case of sub-acute meningitis also noticed. 31% patients were treated with only doxycycline. But rest of the patients required another anti-microbial medication as per co-morbid disorders (Table 5).

## DISCUSSION

In this present study we had documented a case series of scrub typhus cases during month of September, 2019 to March 2020 which were quite

unusual time of occurrence. The extended rainy season and also sporadic unusual rain in winter might be an explanation. Demographic analysis of our study revealed a mixed picture regarding occupation of participants where most active age group was found more vulnerable for scrub typhus. This similar observation was observed in Sinha *et al.* Madi *et al.* and Takhar *et al.* study.<sup>4-6</sup> Females account for 54% and most of them were housewives. Our hospital serves in an area of migrating workers where women usually look after the agricultural works during harvesting time. This could be a possible explanation of this trend. Almost same observation observed in Takhar *et al.* study in Rajasthan.<sup>4</sup> While Rajoor *et al.* reported more men to be affected in his place.<sup>7</sup>

Only two patients had classical Escher or rash in this current study. In Indian context we differ from classical description of scrub typhus with the absence of Escher. This may be due to re-exposure, variation of strains or resistance by indigenous population. Our study supports this finding with other study<sup>8</sup> regarding the absence or less presence of Escher/rashes among South-East Asian scrub typhus patients.

We have also noted positivity of dengue serology in four of our patients and presence of malaria co-infection in one patient which are very much endemic in this area. We had experienced several outbreak of dengue fever for last two to three years which constitutes the major portion of acute febrile illness. Initial presentation of fever, myalgia, tiredness and paucity of rashes makes the initial differential diagnosis very difficult. A significant overlap of presentation and resurgence of scrub typhus in background of dengue endemicity may partly be explained with common behavioral and seasonal pattern. An epidemiological investigation is Needed to be implement to establish the connections. Few studies mentioned presence of co-infection due to common host and environmental factors.<sup>9</sup> Identification of co-infection is very important, as treatment differs significantly for dengue, malaria and scrub typhus. National guideline for dengue fever management discourages use of

antibiotics in dengue fever cases. However, application of antibiotic in early phase of scrub typhus can reduce the mortality. So, it is necessary to include scrub typhus serology test as routine blood test for all AFI patients for this area. Perhaps, diversity of presentation apart from fever and lack of uniformity are the hallmark of scrub typhus presentation. 16% of our participants presented with altered sensorium which is much less than other reported studies.<sup>4</sup> Headache, weakness, nausea were most common presenting complains after fever which were non-specific in nature but similar with Peesapati *et al.* study.<sup>10</sup> Breathlessness and cough were present in 30% and 29% of patients which were observed in severe condition among hemoptysis patients. Our study points towards more respiratory symptoms comparing other reported studies. 20% of our patients showed radiological evidence of plural effusion which was higher than mostly reported studies. Lymphadenopathy and hepatosplenomegaly were present in 07% and 21% in our study respectively which was similar to other studies.<sup>4,5</sup> One study findings have suggested that the presence of generalized lymphadenopathy indicates a late presentation and a worse outcome of scrub typhus cases.<sup>11</sup> Percentage of patient with thrombocytopenia is another conspicuous different picture in this study. We noted only 25% patients with thrombocytopenia in this study. Apart from thrombocytopenia, abnormalities in liver and renal functions in our study matches with other reported in similar studies.<sup>4,10</sup> Only Two patients admitted with sub-acute meningitis and one of them expired after longtime management at Intensive Care Unit (ICU). 9 (11%) patients admitted in emergency with circulatory collapse whereas 12 patients were put on mechanical ventilation. Acute Respiratory Distress Syndrome (ARDS) develops in two patients which was much lower than previously reported.<sup>4,12</sup> Both ARDS patients succumb to death and one patient meet the similar fate after developing acute renal failure. Though the incidence of ARDS and Acute Kidney Injury (AKI) were less than other reported but they stands for most common cause of mortality like similar observational studies.<sup>4</sup> We observed a low mortality rate (4%), which was lower than previously reported 7 to 30 %.<sup>10,13</sup> Facility of tertiary care and increasing awareness among local medical fraternity regarding the disease may be an explanation apart from lower virulence of virus or indigenous resistance as host or environment factor. Most of our patients respond with recommended antibiotic without any adverse reactions which is inspiring in terms of application of complicated second line or third line managements.

## CONCLUSION

With wide spread clinical suspicion of dengue or other fever as etiology of Acute Febrile Illness (AFI) we suggest early screening for scrub typhus as the treatment option for this area can reduce the mortality due to scrub typhus.

## ACKNOWLEDGEMENT

We sincerely thanks to the Dr. Sonali Ghosh, Junior Resident, Department of Medicine, Monmohini Multi-specialty Hospital, Murshidabad for

the kind cooperation extended during the course of the study and also acknowledge cooperation of all patients.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**AFI:** Acute febrile illness; **AKI:** Acute kidney Injury; **ALT:** Alanine Aminotransferase; **ARDS:** Acute respiratory distress syndrome; **AST:** Aspartate Aminotransferase; **CBC:** complete blood count; **Hb%:** Hemoglobin %; **HCV:** Hepatitis C Virus; **HIV-AIDS:** Human Immunodeficiency Virus – acquired Immunodeficiency syndrome; **ICU:** Intensive care unit; **IgM:** Immunoglobulin M; **PTB:** Pulmonary tuberculosis; **RTI:** Respiratory tract infection; **UTI:** Urinary tract infection; **WBC:** White blood cell.

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**Cite this article :** Sarkar K, Acharyya A, Ghosh S, Ghosh M, Bhattacharya A, Ghosh K. Clinical Manifestation and Complications of Scrub Typhus Cases: A Hospital-based Observational Study from Rural Part of West Bengal. *Int J Med Public Health.* 2020;10(4):180-3.