International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 15, Issue 4, 2023

Original Article

AN OUTBREAK OF SCRUB TYPHUS IN A REMOTE VILLAGE-AN OVERVIEW

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Received: 20 Apr 2023, Revised and Accepted: 11 Jun 2023

ABSTRACT

Objective: An outbreak of scrub typhus was declared by Public Health authorities in our district in October, 2022. To investigate this a team of experts from Microbiology, SPM, Medicine and Pediatric Medicine was sent to the place of outbreak and they observed that there was heavy vegetation, stagnant water, dwellings heavily infested with rodent population. There was heavy rain in the past two weeks in the district. To investigate the cause of sudden upsurge of febrile illness cases.

Methods: Blood samples were collected from 28 persons who were symptomatic with fever/headache/diarrhea/rash and myalgia to do tests for Scrub typhus, Typhoid fever, Malaria, Dengue, Complete blood count, CRP, LFT and KFT. The samples which were positive for Scrub typhus in rapid test kits were subjected for IgM ELISA to confirm scrub typhus.

Results: Seven of twenty-eight patients tested positive for scrub typhus by rapid test (25%), and four of them were positive by IgM ELISA (14.28%). Three patients were Widal-positive (10.7%). More than half samples showed increased CRP levels (53.57%). Thrombocytopenia and mild leucocytosis was observed in scrub typhus cases (42.85%) as well as in typhoid cases.

Conclusion: Any outbreak during monsoon should be investigated thoroughly not only for the specified disease but also for all infectious diseases that are prevalent in that area.

Keywords: Scrub typhus, Typhoid fever, Eschar, Infectious diseases, Thrombocytopenia

DOI: https://dx.doi.org/10.22159/ijcpr.2023v15i4.3015. Journal homepage: https://innovareacademics.in/journals/index.php/ijcpr

INTRODUCTION

Scrub typhus, a vector-borne zoonotic infection caused by the bacteria Orientia tsutsugamushi, is one of the most common and clinically important rickettsial infections worldwide. Patients with a febrile illness with or without an eschar confirmed by a molecular/serological diagnostic test are defined as Scrub typhus cases. An estimated one million cases occur annually with a high case fatality rate. Although scrub typhus is a major public health threat in India, the burden and distribution remain unclear. There has been a resurgence of scrub typhus across India in recent years [1].

Scrub typhus is transmitted to humans by the bite of larvae of trombiculid mites [2, 3] and symptoms appear 5–14 d after the bite, include high fever, headache, rash, [3] myalgia, lymphadenopathy, nausea, vomiting, eschar (black spot arises at mite biting site), abdominal pain, and non-specific flu-like symptoms. This infection precedes to severe complications that leads in multiorgan failure, including jaundice, acute renal failure, and disseminated intravascular coagulation (DIC), acute respiratory distress syndrome, myocarditis, and meningoencephalitis [4]. Symptoms of scrub typhus concur with other co-endemic diseases such as leptospirosis, dengue, brucellosis, and typhoid, which makes it more troublesome to differentiate it from others [5]. The presence of eschar at mite biting site is a specific (98.9%) marker for clinical diagnosis of scrub typhus; however, the presence of eschar can be varied extensively in patients from 7 to 97% [6]. The presence of eschar in India and other Asian populations is meagre, which makes it an inappropriate method for the detection of Orientia tsutsugamushi; hence, the diagnosis relies upon laboratory tests [7, 8].

There was the sudden surge of febrile cases with two deaths occurring in a remote village in our district with some positives for scrub typhus, made us to investigate the cause of febrile illness, with all possibilities that cause short outbreaks during monsoon and post-monsoon period.

Aim: To investigate an outbreak of Acute febrile illness

Inclusion criteria

1. Individuals suffering from acute febrile illness/Diarrhea/Rash/Arthralgia and Headache
2. Primary contacts of above Individuals.

Exclusion criteria

1. Individuals with chronic illnesses

MATERIALS AND METHODS

Public Health authorities declared an epidemic of scrub typhus on 20th Oct, 2022, after getting five positives for scrub typhus (done at the private hospital and at PHC with two deaths) in Appapuram village of Laveru Mandalam of Srikakulam district with a history of the sudden appearance of febrile cases within short span of one week and two deaths occurred in the same household, during last two days. One was 76 y old female had a history of fever for which she was treated symptomatically and later developed disorientation for which she was admitted in a private hospital, where she was tested positive for scrub typhus by the rapid method. Her granddaughter, 14 y old, developed fever for one week, got positive for scrub typhus done at PHC, later developed respiratory distress and succumbed before admission.

In this background medical team was constituted with one faculty from each department of Microbiology, SPM, General medicine and Pediatric medicine. The team visited and surveyed the entire village. The team observed that there was heavy vegetation, stagnant water, storage sheds for firewood and cattle dung near dwellings, which are heavily infested with rodent populations. There was heavy rain in the past two weeks in the district resulting in heavy vegetation as well as an increase in insect, mite population. Medical camp was conducted in the village and identified twenty-eight persons who were suffering from with one or more symptoms like fever, rash, diarrhea, arthralgia, myalgia and headache, since last 2-7 d. On physical examination of these symptomatic individuals, eschar was not found in any one of them. After collection of blood samples symptomatic treatment was given with Tab. Paracetamol (650 mg

6th hourly) and Tab. Doxycycline 500 mg/bd. and eighteen patients were admitted in Government General Hospital, Srikakulam, with high-grade fever and follow-up was given.

Blood samples were collected in plain and EDTA tubes to do a battery of tests from symptomatic people under strict aseptic conditions and samples were transported to Dept. of Microbiology for further process. Samples were tested for Scrub typhus, Typhoid fever, Malaria, Dengue, Complete blood count, CRP, Liver function tests and Kidney function tests. As kits are not available for leptospirosis, we were unable to do tests for leptospirosis. The samples which were positive for Scrub typhus in rapid test kits were subjected for IgM ELISA to confirm scrub typhus by sending samples to SVIMS, Tirupati as ELISA it is not available at our Institute.

Scrub typhus Rapid test is an immunochromatographic test from the "ABOTT" Bioline, Rapid diagnostic test kit; we consider it as positive when both the control band and test bands shows pink line.

Table 1: Showing tests performed for the patients and results

S. No.	Age	Sex	Compliants	Occupation	Scrub typhus rapid	Scrub-elisa	Malaria	CRP	Widal
1	55	F	Fever	Ag. worker	N		N	N	N
2	23	M	Fever	Ag. worker	N		N	N	N
3	25	M	Fever	Driver	N		N	1:4	N
4	31	M	Diarrhea, Fever,	Farmer	N		N	1:4	1:80, 1:160
5	30	F	Fever, Headache	Ag. worker	N		N	N	N
6	35	M	Fever, Headache	Ag. worker	N		N	N	N
7	13	F	Fever, Headache	student	N		N	N	N
8	30	M	Fever	carpenter	N		N	1:8	1:80, 1:160
9	63	M	Fever, Headache	Farmer	N		N	N	N
10	60	M	Fever	Ag. worker	N		N	N	N
11	30	M	Fever, Headache	Farmer	N		N	N	N
12	43	M	Fever	Farmer	N		N	N	N
13	48	M	Fever, Pain Abdomen	weaver	N		N	1:8	1:80, 1:160
14	70	M	Fever, Headache	Farmer	Positive	Positive	N	1:16	N
15	36	F	fever, diarrhea	Ag. worker	Positive	Neg	N	1:8	N
16	26	F	Fever	Farmer	N		N	N	N
17	22	M	Fever, rash, Headache	Farmer	Positive	Neg	N	1:8	N
18	42	M	Fever	Ag. worker	N		N	N	N
19	68	F	Fever, Headache	Housewife	N		N	1:16	N
20	56	F	Fever	Ag. worker	N		N	1:8	N
21	28	F	Fever, Headache	Ag. worker	N		N	N	N
22	65	M	Fever, Headache	Farmer	N		N	N	N
23	60	M	Fever	Ag. worker	N		N	1:8	N
24	41	F	Fever, diarrhea, rash	Ag. worker	Positive	Neg	N	1:16	N
25	28	F	Fever,	Housewife	N		N	1:8	N
26	33	M	Fever, Headache	Farmer	Positive	positive	N	1:4	N
27	33	M	Fever, diarrhea	Farmer	Positive	positive	N	1:16	N
28	55	M	Fever, rash, Headache	Farmer	Positive	positive	N	1:16	N

Ag. worker means agricultural worker

Table 2: Showing results of CBC, RFT and LFT

S. No.	Urea	Creatinine	Bilirubin	SGOT (IU/l)	SGPT (IU/l)	ALP (IU/l)	HB (Gms%)	TC/cmm	Platelet count/cmm
1	30 mg/dl	1.2 mg/dl	TB-0.6	22	13	38	11.4	9400	257000
2	20 mg/l	0.6	TB-0.7	20	11	40	14.9	7000	245000
3	18 mg/l	0.5	TB-0.5	20	16	40	13.8	8300	174000
4	32 mg/l	1.1	TB-0.9	30	26	45	13.8	12100	150000
5	24 mg/l	0.8	TB-0.6	11	13	40	10.8	10900	342000
6	20 mg/l	0.7	TB-0.4	13	11	38	18.4	6800	217000
7	20 mg/l	0.6	TB-0.7	13	16	34	13.2	8100	379000
8	20 mg/l	0.8	TB-1.0	30	28	76	15.2	15400	148000
9	30 mg/l	1	TB-0.8	28	20	70	12.5	4100	185000
10	30 mg/l	1.2	TB-0.6	22	16	80	13.1	4300	218000
11	24 mg/l	0.9	TB-0.7	18	16	80	11.6	7100	244000
12	34 mg/l	1.2	TB-0.4	30	28	106	14.2	6100	223000
13	28 mg/l	1	TB-0.8	24	24	42	14.9	14300	151000
14	36 mg/l	1.3	TB-0.8	12	14	80	11.5	13800	133000
15	24 mg/l	0.8	TB-0.6	22	20	102	9.2	13300	290000
16	20 mg/l	0.7	TB-0.9	20	14	44	11.9	6600	364000
17	20 mg/l	0.7	TB-0.6	31	24	70	14.9	11800	369000
18	28 mg/l	0.1	TB-0.7	26	22	84	20	3900	190000
19	30 mg/l	1	TB-0.4	20	16	82	13.9	8100	216000
20	24 mg/l	0.9	TB-0.6	31	28	92	9.9	11100	136000
21	22 mg/l	0.9	TB-0.7	24	20	72	10.9	5200	302000
22	34 mg/l	1.3	TB-0.9	28	20	100	14.1	6000	225000
23	28 mg/l	1.3	TB-0.7	32	29	106	12.8	5100	175000
24	20 mg/l	1.1	TB-0.7	20	18	70	11.9	9500	274000
25	24 mg/l	1.2	TB-0.9	20	18	81	11.7	10900	326000
26	28 mg/l	0.9	TB-0.9	24	20	82	12	15700	175000
27	24 mg/l	1.2	TB-0.7	22	18	92	11.4	14300	218000
28	30 mg/l	1.1	TB-0.7	30	24	70	11.9	12400	22400

CRP was tested by latex agglutination method, using BEACON: Qualitative and Semi-quantitative test kit. Samples that were positive by the qualitative method were tested by a semi-quantitave method. Then CRP concentration was calculated as per the instructions of the manufacturers.

Blood samples were tesed for Malaria Pf/Pv antigens by immunochromatographic technique, using kits from Med source ozone Biochemicals Pvt. Limited. Malarial antigens, LDH (lactate dehydrogenase) and HRP-II (Histidine rich Protein II) were detected by this kit.

Widal slide Agglutination test was used to detect 'O'and'H' antibodies of Salmonella typhi and Para typhi A and B by using 'O'antigens of S. typhi and 'H' antigens of Salmonella typhi, Para typhi A and B; Here the test kit is from the BEACON for both qualitative and semiquantitative measurements. Granular agglutination for"O" and flocculating agglutination for 'H" was considered as positive reaction. Semiquantitative test was done when test was positive byqualitative method. Diagnostic titerof1:80consideras positive.

CBC, RFT and LFT were done using kits respectively in the departments of Pathology and Biochemistry.

RESULTS

Out of 28 cases, 18 were males and 10 were females. Age grouprangingfrom22-70 y. Majority of them (78.4%) are either farmersor agricultural laborers. Among total patients seven were positivefor Scrub typhus by Rapid test, three were positive for Typhoid. Allsamples were negative for malaria and dengue fever as shown intable 1. RFT and LFT tests were within normal range as shown intable 2. Seven of twenty-eight patients tested positive for Scrub typhus byrapid test (25%), and four of them were positive by IgMELISA (14.28%). Three patients were Widal positive (10.7%). More than half samples showed increased CRP levels (53.57%).Thrombocytopenia and mild leukocytosis were observed in Scrub typhuspositive (42.85%) as well as in widal positive cases.

DISCUSSION

Scrub typhus, a common acute febrile illness in India causing severe morbidity, accounts for a large number of deaths [1]. It is grossly underdiagnosed due to lack of clinical suspicion, the presence of non-specific signs and symptoms, and absence of widely available sensitive and specific diagnostic tests [9-12].

There have been reports of sporadic outbreaks of scrub typhus mainly in the eastern and southern Indian states with serological evidence of widespread prevalence of spotted fevers and scrub typhus, particularly during the monsoon and post-monsoon months [10-12]. The rainy season is always favourable for the development of grassland where the proliferation of vectors takes place with an inevitable contact with the human host [10]. Agricultural labourers in the endemic region are known to have a higher risk for developing scrub typhus [13]. The highest risk of scrub typhus was seen in October, December and January, which coincides with the period immediately after the Southeast and Northwest monsoons [14]. During the rainy season, infected chiggers are more frequently found in densely vegetated areas, which is why the condition is also known as river or flood fever [15]. The field rodents and the vector mites act as a reservoir and between the two the infection perpetuates in nature [2].

There was heavy rain in the past two weeks before the outbreak in the district resulting in heavy vegetation as well as an increase in insect, mite and rodent population. Majority of the cases (78.4%) in this study are either farmers or agricultural labourers.

Diagnosis of scrub typhus is challenging as its symptoms mimic with other acute febrile illnesses. Several methods are effectual for diagnosis of scrub typhus that includes enzyme-linked immunosorbent assay (ELISA), immunofuorescence assay (IFA), immunochromatographic test (ICT), Weil–Felix, polymerase chain reaction (PCR) and loop-mediated isothermal amplifcation (LAMP) [8]**.** Mostly rapid testsare used to start treatment immediately and later confirmed by ELISA.

In one study screening for scrub typhus was done by rapid immunochromatographic test to identify antibodies [16]. We used both Rapid method and ELISA for diagnosis. 25% of cases were positive by rapid method, but out of seven positives, only four were confirmed by ELISA (57.14%). Whereas it was 97% correlation between ELISA and rapid method in one study [11].

A high index of clinical suspicion, a careful physical examination, prompt diagnosis and early institution of appropriate antimicrobials as the treatment is simple and doxycycline being the drug of choice, can decrease morbidity and mortality [9, 11, 16, 17].

The presentation of scrub typhus can be variable, often non-specific [18, 19] with symptoms such as fever, gastrointestinal symptoms, headache, myalgia and arthralgia. The disease remains under-diagnosed in our country due to the non-specific clinical presentations which are also commonly seen in other acute febrile illnesses like malaria, enteric fever, leptospirosis and dengue fever [20-22]. Hence testing for above mentioned diseases should be included while investigating acute febrile illness cases.

Majority of patients in the present study presented with a fever with headache and few cases of fever with diarrhoea and some fever with rash. As the symptoms were non-specific, we did test for Scrub typhus, Typhoid, Malaria and Dengue and seven were tested positive for scrub typhus and three for typhoid. Co-infection with malaria and Leptospirosis was reported in one study [17]. But we didn't get any co-infections in these cases.

Identification of eschars in the Indian population is difficult due to dark skin [21, 23]. With incidence ranging from 4% to 46%. Eschar was not found in any case in the present study like Madi D *et al.* study [24]. But it's presence widely varies in different studies (2.3 % in Uday W. Narlawar *et al.* study, [25] less than 4% in Selvaraj Stephen *et al.* study, [23] 4.3% in Shankar V *et al.* study, [16] 8.9% in Sweta Singh *et al.* study, [26] 12.1% in Takhar RP *et al.* study, [12] 13.1% in MVS Subbalaxmi *et al.* study [22] and 20% in Stalin Viswanathan *et al.* study [21]. MVS Subbalaxmi *et al.* emphasised that absence of eschardoes not rule out scrub typhus [22]. The difference in incidence of eschar may also be due to variation in serotypes/endemic strains among the regions [24]. Premaratna *et al.* postulated that in dark-skinned patients early/very small eschar could be easily overlooked [27].

Among the laboratory abnormalities, most common haematological abnormality noted was thrombocytopenia (30.1% in the study of MVS Subbalaxmi *et al.*, 73.91% in Selvaraj Stephen *et al.* study and also in Pathania *et al.* study [19, 22, 23] where as we have observed thrombocytopenia in 42.85% cases and haemoglobin level less than 12 gms/DL in 85.7% of scrub typhus positive individuals.

Scrub typhus is fast emerging as a public health threat [26, 28] and further research to protect the population from this deadly infection is essential. Active surveillance has to be done to understand exact magnitude, epidemiological aspects, and distribution of vector and disease of this reemerging neglected tropical disease [29]. India has experienced a large increase in scrub typhus incidence and documented an expansion in geographic distribution throughout the country [30]. To prevent rickettsial infections, lice, mites, and other vectors need to be controlled with the proper use of an insecticide. For personal prophylaxis, clothes and blanket should be impregnated with benzyl benzoate, and mite repellent (diethyltoluamide) should be used on exposed skin surfaces [15]. Health education campaigns and environmental precautionary measures were suggested to the villagers as dumping of household waste away from the residential house. As there is no vaccine for scrub typhus fever, extensive awareness on fever to healthcare provider and community people is required to prevent scrub typhus transmission [13, 28].

CONCLUSION

Any outbreak during monsoon should be investigated thoroughly not only for the specified disease but also for all infectious diseases that are prevalent in that area.

RECOMMENDATION

Advice was given to health and panchayat authorities to enhance IEC activities, proper garbage disposal, removal of scrub vegetation, spraying of insecticides, supply of protected water

Public were advised to use foot ware outdoors to prevent mite borne infections like scrub typhus, worm infestations like hookworms, schistosomiasis etc, drinking of boiled water during rains to prevent infectious diseases that spread faeco-orally like enteric fever, shigellosis, cholera, enteric hepatitis viruses etc and dispose domestic waste away from dwellings to avoid rodent populations.

Health care providers should be vigilant in the differential diagnosis of febrile illness during outbreaks.

LIMITATIONS OF STUDY

Small study group, unavailability of tests for Leptospirosis and IgM ELISA kits for scrub typhus.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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