Document heading doi: 10.21276/apjhs.2019.6.2.3 **Research Article**

Scrub typhus: an important differential diagnosis of acute and subacute febrile illness

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Abstract

Background: Scrub typhus is an acute febrile illness caused by an obligate intracellular organism *Orientia tsutsugamushi.* The name is derived from the vegetation type that usually harbors the vectors. Scrub typhus is endemic to a distinct region, the tsutsugumashi triangle, which include Japan, Taiwan, China and South Korea.Scrub typhus is known to occur all over India including the north hilly areas. Cases of scrub typhus from State of Bihar are few and that too reported from hospitals of other states. **Objectives:** This study was undertaken to determine the prevalence of scrub typhus in patients presenting with acute and subacute febrile illness, to study the clinical profile and to assess the utility of Enzyme-Linked Immunosorbent Assay for sero diagnosis of scrub typhus.**Methods:** We undertook a retrospective , cross sectional study at a tertiary care super speciality teaching hospital in over a period of 18 months from January 2016 to July 2017**.** Patients presenting with acute and sub-acute undifferentiated febrile illness, admitted in department of general medicine were included in the study **Results:** Out of total 144 admitted patients of acute and sub-acute undifferentiated febrile illness, 18 were found to be suffering from scrub typhus. It was 12.5% of total cases of undifferentiated febrile illness. The disease was prevalent in all age group including old age. 61% of patients with scrub typhus were female and 39% were male. All 18 patients had fever as chief complaint. Other common complaints were chills, myalgia, abdominal pain and yellow discoloration of urine. Eschar were found in five patients.**Conclusions** Early diagnosis is essential to reduce the morbidity and mortality in scrub typhus. Laboratory diagnosis is based mainly on serological tests.

Keywords: Eschar, Fever, Multi-organ, Rickettsia, Scrub typhus.

Introduction

Scrub typhus is a rickettsial disease caused by the organism *Orientia tsutsugamushi.* The organism is transmitted through the bite of larval forms (chiggers) of Trombiculid mite[1].The organism is small, gram negative, obligate intracellular organism whose polysaccharide bears an antigenic relationship to Proteus OX-K antigen which is used in serologic test to confirm scrub typhus[2].

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The vectors are *Leptotrombidium akamushi* in Japan and *Leptotrombidium deliensis* in India. The mite inhabits in mite islands. Four factors are essential for the establishment of a focus of infection, namely coexistence and intimal relationship among *Orientia tsutsugamushi*, chiggers, rats and transitional form of vegetations collectively known as zoonotic tetrad[3].

Only the larval stages of mite suck blood meal. Rodents particularly rats of subgenus *Rattus* are natural hosts for scrub typhus. The field rodent and vector mites act as reservoir and between the two the infection perpetuates in nature. Scrub typhus was first described by Hashimoto from Japan[1].

When human being encroaches the mite-infested area he is prone to get infected accidentally. Scrub growth specially the secondary scrub growth occur after clearance of primary forest. Cases are more common in

rainy season and soon after rainy season. Humans are infected when they trespass onto these mite islands and are bitten by mite larvae. The disease is endemic in the geographical region known as *tsutsugamushi* triangle which include Japan, China, Korea and Taiwan in the north , India and Nepal in the west , Australia and Indonesia in the south[4].

In India, this disease is being reported time to time and known for several decades. Thus the disease is widely spread all over the country and was reported in several states- Haryana, Jammu & Kashmir, Himachal Pradesh, West Bengal, Assam, Maharashtra, Kerala and Tamil Nadu[5]. Although the disease is endemic in our country, it is grossly under-diagnosed due to nonspecific clinical presentation, lack of access to diagnostic facility in most areas and low index of suspicion by clinicians[6].

Methodology

Type of study and study design

It is a retrospective , cross sectional study.

Study population

This study was conducted at a tertiary care superspeciality teaching hospital in Departments of General Medicine and Microbiology at IGIMS, Patna

Duration of the study

18 months from January 2016 to July 2017

Sample size

18 of 144 cases

Inclusion criteria: Patients presenting with acute and sub-acute undifferentiated febrile illness,
admitted in department of general medicine .

Exclusion criteria: Patients diagnosed to have some other associated infection and other causes of acute febrile illness. Patient having co-morbid condition like chronic renal failure, chronic liver disease or patients with known neoplastic disease.

Sample collection and Data collection procedures

A detailed history with special consideration to their occupation and area of residence was obtained. Each patient was subjected to detailed clinical examination with meticulous search for features like rash, eschar, icterus, hepatomegaly and splenomegaly. Basic laboratory tests like complete blood counts, peripheral blood film, absolute platelet count, serum electrolyte, urine complete analysis, liver function tests , kidney function tests and prothrombin time were carried out. In addition, tests such as chest X-ray, abdominal ultrasound and computerized tomography (CT) scan, if required, were done. These patients were also subjected to other tests including blood culture, Widal test, rapid antigen card test for malaria and serology for dengue.

Specific-antibody ELISA

Commercially available ELISA kit (Immune Med Scrub typhus Rapid), which is a qualitative test for the IgG and IgM antibodies against *O. tsutsugamushi* was used (Lateral flow Immuno Chromatographic Assay). After applying dilute serum, plasma or whole blood onto the hole of test device, each reactant diffuses on the membrane to the recombinant antigens marked as test lines, if positive, the test line turns to red colour because antigen- antibody – gold conjugate complex is formed on the test lines.

Ethical considerations: Informed consent was obtained from all the participants. Institutional Ethics Committee (IEC) approval was obtained.

Results

Out of total 144 admitted patients of acute and sub-acute undifferentiated febrile illness, 18 were found to be suffering from scrub typhus. It was 12.5% of total cases of undifferentiated febrile illness. The disease was prevalent in all age group including old age. 61% of patients with scrub typhus were female and 39% were male (Fig 1). Most of the cases were reported in monsoon and early winter season. 15 cases were from rural area and were involved in farming; remaining two were from urban area. One patient had a history of travel from Maharashtra. (Fig 2).All 18 patients had fever as chief complaint. Other common complaints were chills, myalgia, abdominal pain and yellow discoloration of urine. Two patients had significant multiple joint pain and two had hemorrhagic manifestations (Table 1). Eschar were found in 5 patients which were located at axilla, medial side of arm, thigh and scrotum (Fig. 4,5,6). Icterus was present in 6 cases and 5 cases had serositis. Splenomegaly and hepatomegaly were observed among 5 and 3 patients respectively. Hepatitis was the most common complication seen in 10 cases. Acute renal failure was reported among 8 patients. 8 patients were having multi-organ dysfunction. Disseminated intravascular coagulation was seen in one patient but that patient was also suffering from malarial co-infection (Fig 3).

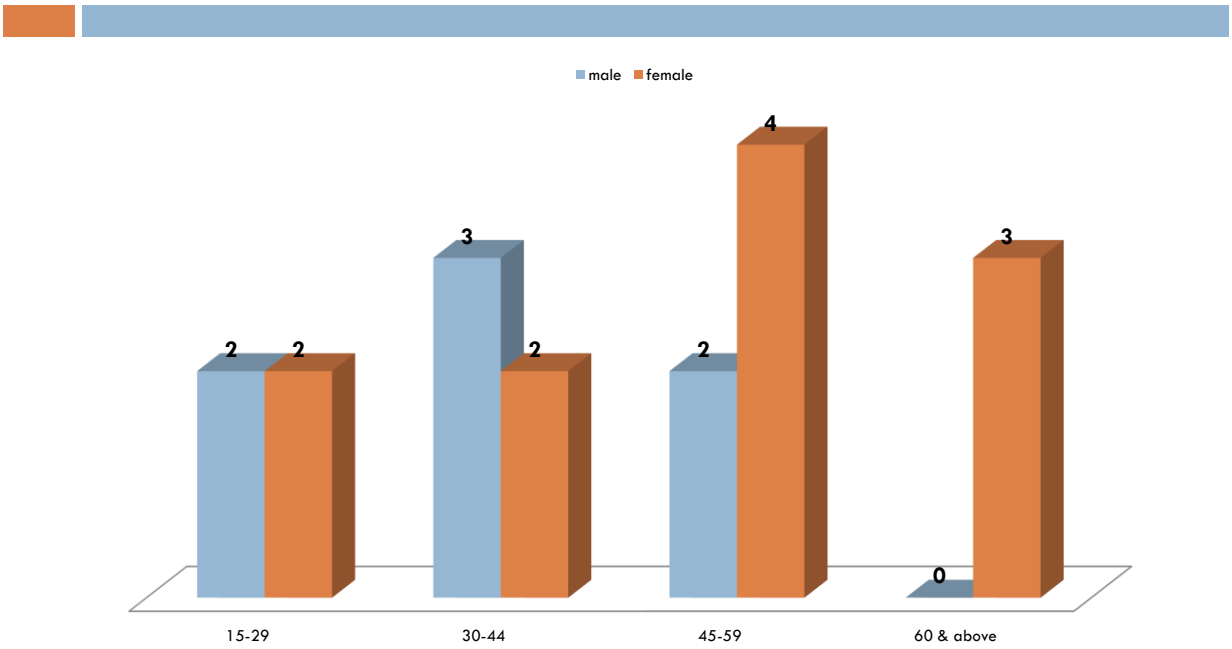

Fig 1:Distribution of patients according to age(years) and sex

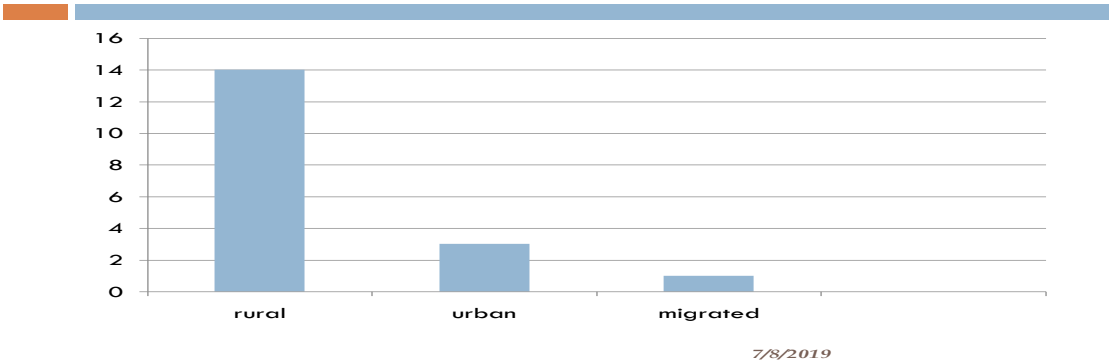

Fig 2: Rural-urban disrtibution

Table 1: Signs and symptoms at presentation

Signs	No.	Symptoms	No.
Eschar	5	Fever	18
Icterus	6	Chills	8
Hepatomegaly	3	Dyspnoea	3
Splenomegaly	5	Myalgia	6
Lymphadenopathy	2	Headache	4
Pleural effusion	3	Pain Abdomen	7
Ascites	3	Diarrhea	3
		Yellow Discoloration of urine	4
		Hemorrhagic manifestation	2
		Joint Pain	2

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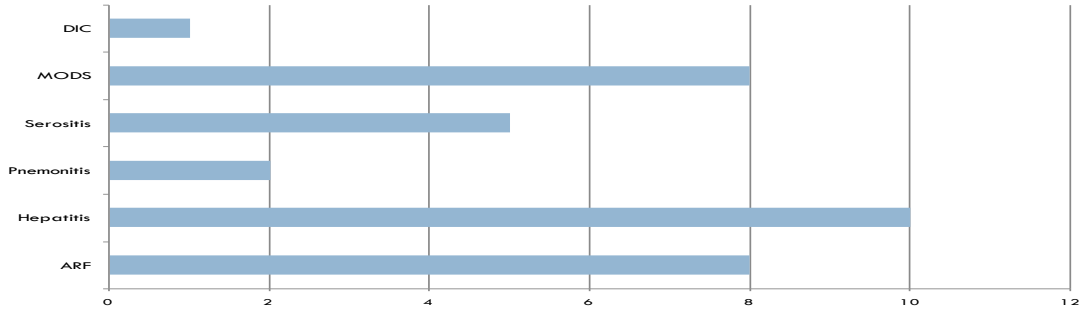

Fig 3:Complications

Discussion

In the present study, the percentage of female patients were higher (61%), than the males (39%) and this trend has also been reported , however Saha et al reported more number of positive male patients in their study[7]. Illness varies from mild and self limiting to fatal one[8]. After an incubation period of 6-21 days, onset is characterised by fever, headache, myalgia, cough, anorexia and GI symptoms. Initially most of the symptoms are similar to symptoms of common febrile illnesses like malaria, typhoid, and dengue. O. *tsutsugamushi* invades endothelial cells to produce disseminated vasculitis and perivascular inflammatory lesion , which results in significant leakage and ensuing end – organ injury of various organ system. It presents as either nonspecific febrile illness with constitutional symptoms or with organ dysfunction involving kidney, liver, lung, CNS or with circulatory collapse and hemorrhagic features.

Scrub typhus is one of the differential diagnosis in patients with hemorrhagic fever especially associated with jaundice and/ or renal failure[9].The chigger phase of mite get attached to skin of host and prefer to

feed where skin is thin and wrinkled. Large number of organism are injected into its host when it feeds. In many patients skin lesion, black eschar, develop at the site of chigger attachment. The site bitten by mites form characteristic eschars with regional lymph node enlargement and maculopapular rash. It is one of the clinical diagnostic clue of scrub typhus but not seen in all patients. Presence of eschar has been shown to be an important finding for diagnosis of rickettsial pox, scrub typhus and other mite or tick borne rickettsiasis[10,11]. .Eschars are painless, small punched out ulcers , with a black necrotic centre resembling the mark of a cigarette burn, which is surrounded by an erythematous margin. Eschar on moist intertriginous surfaces may be missed because these may lack the black scab, and appear as shallow yellow based ulcers. Scrub typhus has a broad clinical spectrum from mild infection to multi-organ failure. Fever is most common presentation along with chills and myalgia. This disease is under-diagnosed in many parts of India including Bihar because of very low index of suspicion and lack of diagnostic facilities. In scrub typhus, complications usually develop after few days of febrile illness. Jaundice, renal failure, pneumonitis, ARDS, septic shock, myocarditis and meningo-encephalitis are various complications known with this disease[12,13]. In a study done by Sariga et al[14], fever was the most common symptom (92.9%) in keeping with our study. Hepatitis was the most common complication seen in our study followed by acute renal failure and multi-organ dysfunction According to Sariga et al[14] , the most common complication found in the patients with scrub typhus was acute respiratory distress syndrome (15.9%). Other complications like hepatic dysfunction, pleural effusion and meningoencephalitis were noted.

If not diagnosed and treated promptly then this disease may lead to higher morbidity and mortality.

All patients were treated with cap. Doxycycline (100mg) twice daily for seven days. In our study there was no mortality. All patients were discharged in healthy condition except one who left hospital against medical advice.

Conclusion

This study shows that scrub typhus is also prevalent in Bihar and it must be suspected in all cases of undifferentiated acute and subacute febrile illness. Presentation with multiple joint pain is an unusual finding. Scrub typhus is an important differential diagnosis of dengue fever and malaria because of similar clinical features and seasonal variation . If diagnosed early, treatment is effective with a favorable outcome

Fig 4:Calf

Fig 5:Axilla

Fig 6:Scrotum

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