International Journal of Contemporary Pediatrics
Gupta VK et al. Int J Contemp Pediatr. 2016 Aug;3(3):943-948
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20162370

Research Article

Clinical profile of scrub typhus in relation with malaria and dengue seasonal outbreak from semi desert area of Rajasthan, India

Virendra Kumar Gupta[1]*, Prashant Agrawal[2], Raj Kumar Gupta[3], Ram Babu Sharma[3], Jitendra Prashad Bhatnagar[1]

[1]Department of Pediatrics, NIMS University, Jaipur, Rajasthan, India
[2]Department of Pediatric Cardiology, Medanta hospital, Gurgaon, Haryana, India
[3]Department of Pediatrics, SMS Medical College, Jaipur, Rajasthan, India

Received: 21 April 2016
Revised: 08 June 2016
Accepted: 08 June 2016

***Correspondence:**
Dr. Virendra Kumar Gupta,
E-mail: vk.hindustani@gmail.com

ABSTRACT

Background: Scrub typhus is a zoonotic disease caused by rickettsial bacteria Orientia tsutsugamushi. The disease is endemic in many parts of India. Recent appearance of cases from semi desert district of Rajasthan is highly concerning. The aim and objectives of the study was to present epidemiological demographic profile and distribution, clinical manifestation, laboratory Findings and treatment outcomes of scrub typhus in children.
Methods: A hospital based cross sectional observational stud, ten cases were included having positive IgM antibody against Orientia tsutsugamushi. Their clinical details were taken along with complete physical examination. Laboratory testing included complete blood count, liver function tests, renal function tests, urine analysis, blood & urine cultures.
Results: Of ten children, mean age were 9.7±2.40 years, male, female ratio 1.5, mean duration of hospital stay 7±2.35 days. Fever (100%) was most common presenting symptom and mean duration was 6.8±2.78 days. Other features were tachycardia (80%), tachypnoea (70%), heptoslenomegaly (70%), swelling (60%), vomiting (60%), abdominal pain (40%), rashes (40%), bleeding (30%) and seizures (20%). Thrombocytopenia (80%) and mild elevated liver enzymes were present in most of the cases. Eschar was present only in two (20%) cases. Nine cases were successfully treated with doxycycline and one mortality due to CNS involvement.
Conclusions: Our study emphasizes that pediatric scrub typhus should be suspected when patient presents with high grade fever with heptoslenomegaly with or without eschar mark along with thrombocytopenia and elevated liver enzymes. Early diagnosis could reduce the morbidity and mortality. Drugs useful are Doxycycline, Azithromycin or Chloramphenicol.

Keywords: Scrub, Zoonotic, Eschar, Thrombocytopenia, Heptoslenomegaly

INTRODUCTION

Scrub typhus or tsutsugamushi fever is an acute febrile illness caused by *Orientia tsutsugamushi*, a tiny parasite about the size of bacteria that belongs to the family Rickettsiaceae. Scrub typhus was first described by Hashimoto from Japan in 1899.[1] The term scrub is used because of the type of vegetation (terrain between woods and clearings) that harbours the vector; however, the name is not entirely correct because certain endemic areas can also be sandy, semi-arid and mountain deserts.[2,3]

Scrub typhus is endemic to a part of the world known as the "tsutsugamushi triangle" (Figure 1), which extends from northern Japan and far-eastern Russia in the north,

to northern Australia in the south, and to Pakistan and Afghanistan in the west.[4] The disease is largely limited to South eastern and Eastern Asia, Northern Australia, India, Pakistan, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Ceylon and other islands in the region. In India, it is present in whole of the Shivalik ranges from Kashmir to Assam, Eastern and Western Ghats and the Vindhyachal and Satpura ranges in the central part of India. There were reports of scrub typhus outbreaks in Himanchal Pradesh, Sikkim and Darjeeling (West Bengal) during 2003-2004 and 2007. Outbreaks of scrub typhus are reported in southern India during the cooler months of the year.[5]

Transmission and life cycle

The infection is transmitted to man and rodents by some species of infective trombiculid mites ("chiggers", Leptotrombidiumdeliense and others) which feeds on lymph and tissue fluid rather than blood .The mite is very small(0.2-0.4mm) and can only be seen through a microscope or magnifying glass.[7] Once they are infected in nature by feeding on the body fluid of small mammals, including the rodents, they maintain the infection throughout their life stages and, as adults, pass the infection on to their eggs in a process called trans ovarian transmission. Similarly, the infection passes from the egg to the larva or adult in a process called transtadial transmission. In this way, chiggermite populations can autonomously maintain their infectivity over long periods of time.[6,7]

Rather than biting or piercing the skin, mite larvae prefer to insert their mouthparts down hair follicles or pores. A large numbers of the Orienta tsutsugamushi are present in the salivary glands of the larvae and these are injected into its host when it feeds.[7] The bite of the mite leaves a characteristic black eschar that is useful to the doctor for making the diagnosis.[7] Human infection takes place when man accidentally picks up an infective larval mite while walking, sitting, or lying on the infested ground. The adult mites have a four-stage lifecycle: egg, larva, nymph and adult. The larva is the only stage (chigger) that can transmit the disease to humans and other vertebrates, since the other life stages (nymph and adult) do not feed on vertebrate animals. Both the nymph and the adult are free-living in the soil.[6,7]

After the initial infection the rickettsial spreads systemically and the infected person develops various symptoms like high grade fever, malaise, myalgia, rash, cough, lymphadenopathy, hepatomegaly and splenomegaly and gastrointestinal disturbances including abdominal pain, vomiting, and diarrhea A single or multiple painless escher with an erythematous rim at the site of the chigger bite is seen and thrombocytopenia, and leucocytosis is observed.

The aim and objectives of the study was to present epidemiological demographic profile and distribution, clinical manifestation, laboratory Findings and treatment outcomes of scrub typhus in children.

METHODS

This hospital based, observational study conducted in the Department of Pediatric Medicine, SPMCHI, SMS Medical College, Jaipur.

This study describes the epidemiologic and clinical profile of ten consecutive scrub typhus positive children patients who were admitted. After complete physical examination, routine laboratory investigations like complete blood count, liver function tests, and renal function tests were done in all patients. Urine analysis, peripheral smear for Malaria parasite, Dengue serology, Widal test, blood culture and urine culture were done in all the patients. In all cases diagnosis was based on detection of antibody or IgM against Orientia tsutsugamushi using a single step rapid immunochromatographic assay.

RESULTS

Among the ten patients six were males and four were females, nine patients were from rural areas and one from urban area, all patients were from north east area of Rajasthan. Their mean age was 9.7yr.(Range 5-13 yr.) The duration of illness before hospitalization were4-12 days with an average of 6.8days. Provisional diagnosis of 5 cases were dengue virus infection ,2 cases Malaria, one case as prolonged fever, one case as Meningoencephalitis and one case assumed mixed malaria and scrub typhus.

The most common clinical presentation was fever with chills and rigor which was present in all cases, and other presentation were vomiting in 6 cases (60%),swelling in 6 cases (60%), abdominal pain in 4 (40%), respiratory distress in 4 (40%), bleeding in 3 cases (30%) and seizure with altered sensorium in two patient in case no3& 9 (20%). On examination finding were splenomegaly in 7 cases (70%), hepatomegaly in 7 patient (70%), edema in 6 patient (60%), lymphadenopathy in 3 cases(30%) only two patient had eschar (20%), three patient were pallor . Other physical findings, tachycardia were in eight patient (80%) and tachypnea in 7 patients (70%), ARDS developed in patients No 4. And two patients complicated as shock and two CNS manifestations.

Eight patient had thrombocytopenia (platelet count <100,000/mm3), average 74800 cells/mm3 (range24000-216000), three patient were anaemic out of them one patient had blood transfused, Leukocyte count ranged from 1870-27900cells/mm3 with an average of 10443 cells/mm3. Neutrophilia (PMN > 60%) was found in 50% patients. Lymphocytosis (lymphocyte >40%) in30%and atypical lymphocytosis (atypical lymphocyte>5%) occurred in one patient. Haematocrit were raised in four patients (more than three times on hemoglobin), Abnormal SGOT and SGPT levels were detected in

80%and 70% of all cases and the mean values were 117.79 and 111.55 U/L, respectively. BUN and creatinine were raised in 3 patients. Blood for Widal agglutinin was negative for all cases.

Two patients were positive for malaria mixed infection one by card test and one by PBF examination and patient were positive for Dengue serology for IgG and IgM. Encephalitis developed in case No3 and 9. History of fever and one day of generalized seizure.

Table 1: Clinical status and therapeutic outcome of patients.

Case	1	2	3	4	5	6	7	8	9	10
Age/sex	5y/M	9y/F	10 y/ M	13 y/F	12y/M	11 y/M	12 y/M	8 y/ F	8 y/F	9 y/ M
Resident	Rural	Rural	Rural	Urban	Rural	Rural	Rural	Rural	Rural	Rural
Duration of illness	6 d	10 d	5 d	4 d	5 d	12 d	10 d	5 d	5 d	6 d
Hospital stay	6 d	10 d	12 d	7 d	7 d	7 d	4 d	6 d	6 d	5 d
Fever Chills/Rigor	+ +	+ +	+ +	+ +	+ +	+ +	+ +	+ +	+ +	+ +
Rashes	5th d	-	5th d	-	-	3rd d	5th d	-	-	-
Eschar Mark	-	-	+	-	-	+	-	-	-	-
Swelling	8th d	5th d	6th d	-	3rd d	-	4th d	4th d	-	-
Resp. Distress	-	5th d	-	3rd d	5th d	-	-	-	6th d	-
Epigastrial Pain	-	5th d	9th d	1st d	3rd d	-	-	-	-	-
Vomitting	5th d	5th d	3rd d	3rd d			5th d	-	2nd d	-
Seizure	-	-	4th d	-	-	-	-	-	5th d	-
Bleeding	-	9th d	8th d	-	4th d	-	-	-	-	-
Conjunctival Congestion	-	+	-	+	-	-	-	-	-	-
Hepatomegaly	-	+	+	+	+	+	-	+	-	+
Spleenomegaly	+	+	+	-	+	+	+	+	-	-
Lymphadenopathy	+	-	-	+	+	-	-	-	-	-
Tachycardia	+	+	+	+	+	+	+	-	+	-
Tachypnoea	+	+	-	+	+	+	+	-	+	-
Shock	-	-	-	+	-	+	-	-	-	-
Thrombocytopenia	+	+	+	+	+	+	+	-	-	+
Chest Xray	N	B/l infil. Pl. eff.	N	B/l infil.	B/l infil. Pl.eff	N	N	B/l infil. Pl.eff	B/l infil.	N
Provisional diag.	Malaria	Dengue	Malaria	Dengue	Dengue	PUO	Malaria ? scrub	Dengue	Meningo	Dengue
Associated Pathoogy	Nill	Nill	Mal.	ARDS	Nill	Nill	Mal.	Dengue	N	N
Scrub typhus Diagnosis By	IgM	IgM IgG	IgM	IgM	IgM	IgM IgG	IgM IgG	IgM IgG	IgM IgG	IgM IgG
Treatment	Doxy	Doxy	Chlor. Artes.	Azit. Doxy	Doxy	Doxy	Doxy Artes.	Doxy	Azit. Acycl. Artes.	Doxy
Symptom relief	48 hr	48 hr	72 hr	48 hr	48 hr	72 hr	48 hr	72 hr	Death	48hr

Seven patient were treated with Tab. Doxycycline (4 mg/ kg/ day divided by two doses) and case no 3 were treated with Inj. Chloramphenicol (25 mg /kg / dose IV QID) and case no 4 treated with Inj. Azithromycin (15 mg/kg/day IV OD) initially for 24-48 Hrs due to lack of oral acceptance and switch over to oral Doxycycline after oral intake improved, all patient were successfully treated with these drugs, Case no. 9 were also treated with Inj. Azithromycin (15 mg/kg/day IV OD), Acyclovir, artesunate, clindamycin but not respond to the treatment and required mechanical ventilation later on final result were death on day 6th of hospital admission. The effervescence occurred within 2 and 3 days except case no 9.

DISCUSSION

In many countries of Asia Scrub typhus is widely endemic. Recently, many reports of scrub typhus from different parts of India have been published.[1,8-11] A two-

year nationwide study in Thailand by Leelarasamee A et al showed that 7.5% of patients with acute undifferentiated febrile illness (AUFI) were caused by scrub typhus.[12] Most of the patients in the present study were school-aged and predominantly male children, similar to previous studies.[13-16] Although the clinical manifestations of scrub typhus in children often lacks the classical features, are nonspecific and may be misdiagnosed.

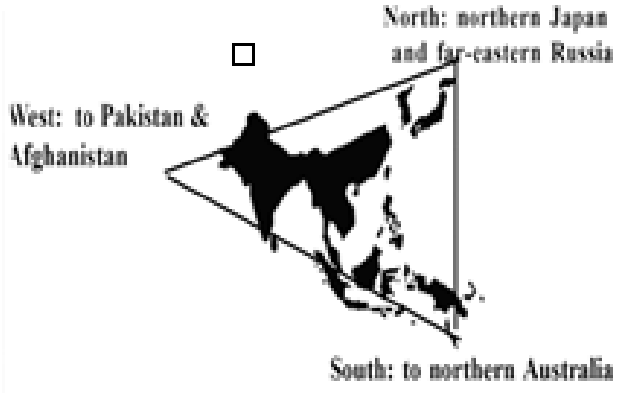

Figure 1: Tsutsugamushi triangle.

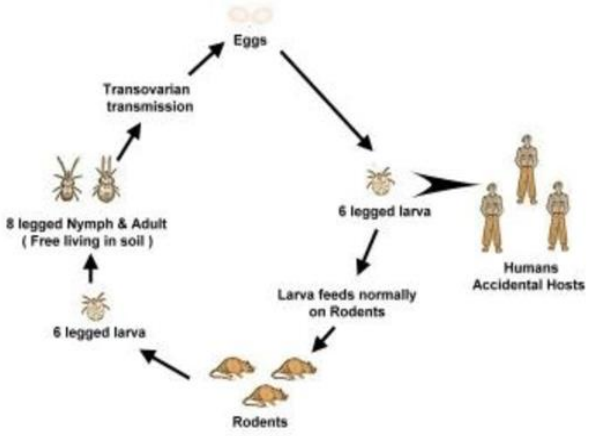

Figure 2: Life cycle of Orientia tsutsugamushi.

Scrub typhus may become a major public health problem in Rajasthan; in the recent or coming years, because a number of cases reports recently from different part of Rajasthan (Unpublished). It is still not known whether scrub typhus is a newcomer or it was previously undiagnosed because it is possible that it existed in this state but went unnoticed as physicians failed to recognize it. Many physicians might have been treating their patients with scrub typhus without considering it in their differential diagnoses as it responds to commonly used antibiotics like doxycycline, chloramphenicol and azithromycin.

However the clinical course of scrub typhus is nonspecific and patient misdiagnose, in the presented study all patient had history of Fever with chills and rigor and thrombocytopenia may be suspicious for scrub typhus in endemic region.

A study done by Chantaet al shows that eschars, a pathognomonic sign of scrub typhus, were present in 75% of the presented patients and were usually painless and single, and a study done by Sudhakar MK et al shows all patient of diagnosed scrub typhus had eschar mark, is differ from our study where only two patient (20%) had eschar mark at multiple site.[17,18] So the suspect ion of the disease could not be made on the basis of escar mark only.

In present study a patient develop ARDS with Respiratory distress, These findings similar from that reported by Punyagupta S and Pothirat C in which complications were those of the acute respiratory distress syndrome from disease process.[19,20]

Shock is another complication of scrub typhus and occurred in two cases of the present study. In the present study, CXR abnormalities were documented in 5patients of patients and consistent with those reported in other studies.[15,21]

Central nervous system (CNS) involvement is another major complication of scrub typhus and occurs in about 2-5%.[13] The manifestations range from aseptic meningitis to meningoencephalitis, and focal neurological signs are rare. In the present study, two cases who presented with fever with multiple episodes of seizure with altered behaviour may reflect the generalized cerebral involvement due to scrub typhus.

In the present study, most patients had mild to moderate elevation of SGOT and SGPT levels (SGOT had higher levels than SGPT), These findings are nonspecific and may occur in other systemic infections e.g. .Dengue infection.[13,22]

The clinical manifestation including pyrexia, heptoslenomegaly and thrombocytopenia are nonspecific and may occur in other systemic infections e.g. Dengue infection, malaria, typhoid etc. Thus, physicians may sometimes have difficulties to give correct diagnosis.

In our study two cases (case no. 3 and 7) were diagnose as a case of cerebral malaria and mixed malaria on the basis of card agglutinin test and PBF examination respectively they were initially treated with anti-malarial but due to not responding or deteriorating the general condition of the child, and one patient case no 8 were diagnose as a case of Dengue fever on the basis of positive serology IgG and IgM and raised haematocrit value were not respond to initial treatment, than we suspect the another co-existence with scrub typhus and go for investigation, all of them were positive, IgM antibody for scrub typhus and treated with chloramphenicol and Doxycycline, they were get successfully respond with these antibiotics and afebrile within 48-72hrs. On the

basis of these cases we should kept in mind co-existence of malaria and Dengue fever with scrub typhus if not responding initially in scrub typhus endemic region.

The Weil-Felix test, which is widely used in many hospitals, lacks sensitivity. A previous study by Chouriyagune C et al found that the Weil-Felix test was positive with acute sera in only 15% of adult cases.[23] So the Weil-Felix test should not be used as a screening test for diagnosis of scrub typhus.

Although rickettsiae can be isolated from or detected in clinical specimens, serological tests still remain an indispensable tool in the diagnosis. Microimmunoflourescence is considered the test of choice. Latex agglutination, indirect hemagglutination, immunoperoxidase assay, ELISA, and polymerase chain reaction are other tests available. In our study all cases were diagnosis on the basis of positive IgM and IgG ELISA based on rapid immunochromatographic assay, which has higher specificity and sensitivity then Weil-Felix test.

Watt G et al shows that adult patients with scrub typhus responded poorly to antibiotics.[24] Doxycycline and chloramphenicol were successfully used to treat pediatric, scrub typhus in our cases and other studies.[14,15] This may be due to the fact that patients were infected with different strains of *O tsutsugamushie.*

This original study is a case series of pediatric scrub typhus. The major disadvantage of this study is limitation of the number of patients in a short duration of study. Thus, the data cannot be generalized, and a larger study should be performed to evaluate clinical feature sand therapeutic outcome.

CONCLUSION

Our study emphasizes the fact that pediatric scrub typhus should be suspected when a patient present with high grade fever with heptoslenomegaly with or without eschar mark and laboratory evidences of thrombocytopenia. The most common complication is acute lung injury and diffuse interstitial lung infiltration was the most frequent CXR findings. Early diagnosis of the disease by appropriate method could reduce the morbidity and mortality. Doxycycline, Azithromycin and chloramphenicol were successfully treated, the patient.

This case series reports shows that scrub typhus are emerging threats in Rajasthan. This febrile illness affects previously healthy active persons and if undiagnosed or diagnosed late may prove to be life threatening.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Mahajan SK. Scrub Typhus. JAPI. 2005;53:954-58.
2. Tamura A, Ohashi N, Urakami H, Miyamura S. Classification of Rickettsia tsutsugamushi in a new genus, Orientia gen nov, as Orientiatsutsugamushi comb. Int J SystBacteriol. 1995;45:589-91.
3. Padbidri VS, Gupta NP. Rickettsiosis in India: A review. J Indian Med Assoc. 1978;71:104-07.
4. Devine J. A Review of Scrub Typhus Management in 2000- 2001 and Implications for Soldiers. J Rural and Remote Environmental Health. 2003;2:14-20.
5. Liu YX, Feng D, Suo JJ. Clinical characteristics of the autumn-winter type scrub typhus cases in south of Shandong province, northern China. BMC Infect Dis. 2009;4;9:82.
6. Lai CH, Huang CK, Chen YH. Epidemiology of acute q Fever, scrub typhus, and murine typhus, and identificationof their clinical characteristics compared to patients with acute febrile illness in southern taiwan. J Formos Med Assoc. 2009;108(5):367-76.
7. Suputtamongkol Y, Suttinont C, Niwatayakul K. Epidemiology and clinical aspects of rickettsioses in Thailand. Ann N Y Acad Sci. 2009;1166:172-9.
8. Chaudhry D, Garg A, Singh I, Tandon C, Saini R. Rickettsial diseases inHaryana: Not an uncommon entity. J Assoc Physicians India 2009;57:334-7.
9. Mathai E, Rolain JM, Verghese GM, Abraham OC, Mathai D, Mathai M, et al. Outbreak of scrub typhus in southern India during the cooler months. Ann N Y Acad Sci. 2003;990:359-64.
10. Prabagaravarthanan R, Harish BN, Parija SC. Typhus fever in Pondicherry. J Commun Dis. 2008;40:159-60.
11. Ittyachen AM. Emerging infections in Kerala: A case of scrub typhus. Natl Med J India. 2009;22:333-4.
12. Leelarasamee A, Chuprapawan C, Chenchittikul M, Udompanthurat S. Etiologies of acute undifferentiated febrile illness in Thailand. J Med Assoc Thai. 2004; 87: 464-72.
13. Silpapojakul K, Chupuppakarn S, Yuthasompob S,Varachit B, Chaipak D, Borkerd T, et al. Scrub andmurine typhus in children with obscure fever inthe tropics. Pediatr Infect Dis J. 1991;10:200-3.
14. Sirisanthana V, Puthanakit T, Sirisanthana T. Epidemiologic, clinical and laboratory featuresof scrub typhus in thirty Thai children. Pediatr Infect Dis J. 2003;22:341-5.
15. Sornchai P, Kanjanavanit S. Pediatric scrub typhusin Nakornping Hospital. Thai J Pediatr. 2000;39:20-9.
16. Sirisanthana V, Poneprasert B. Scrub typhus in children at Chiang Mai University Hospital. J Infect Antimicrob Agents. 1989;6:22-7.
17. Chanta C, Chanta S. Clinical Study of 20 Children with Scrub Typhus at Chiang Rai Regional Hospital. J Med Assoc Thai. 2005;88(12):1867-72.
18. Sudhakar M K, Amarabalan Rajendran Scrub Typhus in Adults – A Case Series from a Tertiary

Care Hospital. Int J Med Public health. 2011;1(2):34-6.
19. Punyagupta S. Cardiopulmonary complication in an acute febrile patient. J Infect Dis Antimicrob Agents 1985;2:194-7.
20. Pothiratana C. Scrub typhus pneumonia with adult respiratory distress syndrome. J Infect Dis Antimicrob Agents. 1987;4:68-72.
21. Choi YH, Kim SJ, Lee JY, Pai KY, Lee YS. Scrub typhus: radiological and clinical findings. Clin Radiol. 2000;55:140-4.
22. Takada N, Khamboonruang C, Yanaguchi T, Thitasut P, Vijrasthira S. Scrub typhus and chiggersin northern Thailand. Southeast Asian J Trop Med Public Health. 1984;15:402-6.
23. Chouriyagune C, Watt G, Strickman D, Jinasen R. The Weil-Felix test for the diagnosis of scrub typhus in Thailand. Intern Med. 1992;8:29-33.
24. Watt G, Chouriyagune C, Ruangweerayud R. Scrub typhus infections poorly responsive to antibiotics in northern Thailand. Lancet. 1996;348:86-9.

Cite this article as: Gupta VK, Agrawal P, Gupta RK, Sharma RB, Bhatnagar JP. Clinical profile of scrub typhus in relation with malaria and dengue seasonal outbreak from semi desert area of Rajasthan, India. Int J Contemp Pediatr 2016;3:943-8.