

Scrub typhus: Clinical spectrum and outcome

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Abstract

Background: Scrub typhus is one of the differential diagnoses for fever with thrombocytopenia. ARDS associated with Scrub typhus has high morbidity and mortality. **Aims:** To evaluate clinical features, lab values, and outcome in patients with scrub typhus and comparison in patients with or without ARDS. **Methods:** A prospective observational study was conducted on 109 patients with febrile illness and thrombocytopenia during a period of 12 months. All 109 patients were tested with both Immune-chromatography test and Weil felix test. Patients having either Immune-chromatography test/Weil felix test positive have been included and considered as scrub typhus positive whereas negative for both Immune-chromatography and Weil felix test were excluded. Clinical features, lab parameters, and outcome were evaluated in all patients with scrub typhus. Statistical analysis used in this study was T-test. **Results:** Among 58 patients who were included (After exclusion of 51 patients among total of 109 patients) 34 patients had no ARDS and 24 patients had ARDS. The clinical feature like dyspnoea, cough, low blood pressure (MAP < 65 mmHg), IVC collapsibility (by ultrasound) and laboratory parameters like decreased Hemoglobin, Hematocrit, Serum albumin, and increased serum creatinine, serum total bilirubin, SGOT, SGPT, LDH, CPK, and serum lactate were statistically significant ($P < 0.0001$) in scrub typhus patients group with ARDS. The higher titers of Weil-felix can be correlated with more severe form of disease according to our observation. All 34 Scrub typhus patients without ARDS recovered completely. Among 24 Scrub typhus patients with ARDS, 22 patients recovered, and 2 patients died. **Conclusion:** Scrub typhus is an important differential diagnosis in a patients having fever with thrombocytopenia. Scrub typhus associated with ARDS has high morbidity and mortality. Early diagnosis and treatment with doxycycline can prevent the occurrence of ARDS

Keywords: Acute respiratory distress syndrome, immunochromatography test, screening criteria, scrub typhus, thrombocytopenia, Weil-Felix test

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Introduction

Scrub typhus is a mite borne acute infectious disease caused by *Orientia tsutsugamushi*.^[1] The term scrub means the type of vegetation (Terrain between woods and clearings) that harbors the vector and typhus means "fever with stupor" or smoke in Greek. "Tsutsugamushi" means small and dangerous, and "mushi" means

insect or mite. Humans are accidental hosts. It affects people of all age. Scrub typhus is endemic in so called "tsutsugamushi triangle" such as Japan, Taiwan, China, and South Korea on the north, India and Nepal on the west, and Australia and Indonesia in the south.^[2]

A billion people are at risk, and nearly a million cases are reported every year.^[3] *O. tsutsugamushi* is an obligate intracellular Gram-negative bacterium; it grows freely in the cytoplasm of infected cells since it lacks vacuolar membrane. It has 5 major serotypes - Boryon, Gilliam, Karp, Kato, and Kawazaki. Scrub typhus is one of the differential diagnosis for fever with thrombocytopenia or hemorrhagic fever.^[4] Scrub typhus can manifest with either nonspecific febrile illness or constitutional

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symptoms (Fever, rash, myalgia, and headache) or with organ dysfunction such as kidney (acute kidney injury [AKI]), lungs (acute respiratory distress syndrome [ARDS]), heart (Myocarditis), liver (hepatitis) and central nervous system (Meningitis).^[5]

The mortality of scrub typhus in untreated patients range from 0% to 30% and tends to vary with age and region of infection. The involvement of lungs has been described which range from bronchitis and interstitial pneumonitis to ARDS. ARDS is one of the serious complications of scrub typhus, which has high morbidity and mortality. The occurrence of ARDS is high in scrub typhus patients who were diagnosed late and received antibiotics late.^[3,6]

This study may be useful in the early diagnosis of scrub typhus (using clinical features and initial lab values) so that the early initiation of specific antibiotic (Doxycycline) can prevent the occurrence or reduce the severity of ARDS.

Materials and Methods

After informed consent either from patient or patient attender (in case where patient is not able to give consent) and ethical clearance from the institutional ethical committee, a prospective observational study was conducted on 109 patients with febrile illness and thrombocytopenia during a period of 12 months between June 2012 and May 2013 in Acute medical care unit of a super specialty hospital. All 109 patients were tested with both immune-chromatography test (ICT) and Weil-Felix test (WFT). Patients having either ICT/WFT (of 1:80 titer and above) positive have been included and considered as scrub typhus positive whereas negative for both immune-chromatography and WFT were excluded from this observational study. 51 patients were excluded as they were negative for both ICT/WFT and remaining 58 patients were positive for either ICT/WFT.

Clinical features, lab parameters, and final outcome were evaluated in these patients. Area of residence (Andhra Pradesh),^[7] detailed clinical examination, presence or absence of eschar, rash and lymphadenopathy were noted. Routine basic labs were sent for all patients. Tropical and other co-endemic diseases such typhoid, Dengue, Leptospirosis and Malaria tests were done in all patients. Additional tests such as ultrasonography of abdomen, Arterial blood gas analysis, chest X-ray, electrocardiogram, two-dimensional echocardiogram, cerebrospinal fluid study, electroencephalography, computed tomography/magnetic resonance imaging brain, blood, and sputum/

bronchoalveolar lavage cultures, etc., were sent as indicated. WFT and ICT done for all cases. APACHE-II and sequential organ failure assessment (SOFA) were calculated for all these patients.

Diagnosis of ARDS was based on criteria for ARDS by Berlin definition.^[8] (1) Onset within 1-week of a known clinical insult or new or worsening respiratory Symptoms, (2) Bilateral lung opacities - not fully explained by effusions, lobar/lung collapse, or Nodules, (3) Pulmonary edema not fully explained by cardiac failure or fluid overload need objective assessment (echocardiography) to exclude hydrostatic edema if no risk factor present, (4) $\text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg with positive end expiratory pressure or continuous positive airway pressure ≥ 5 cm H_2O). Doxycycline was administered for all patients with proved scrub typhus. Various complications associated with disease (AKI, hypotension, ARDS, hepatitis, meningitis) were managed accordingly.

Results

Among 58 patients proved to be having positive for scrub typhus, 24 patients had ARDS and 34 patients had no ARDS. The clinical features and lab values have been compared among these groups. Table 1 shows the clinical characteristics of scrub typhus patients. The incidence of AKI, acute hepatitis and delay in starting treatment with doxycycline were significant in ARDS scrub typhus group compared to non ARDS scrub typhus group.

Table 2 shows $\text{PaO}_2/\text{FiO}_2$ ratio, Intensive Care Unit (ICU) length of stay, and severity of infection. In our observational study among 24 patients with ARDS (mild ARDS: 8 patients, moderate ARDS: 16 patients, and severe ARDS: 2 patients) the lung injury score, intubation rate, ventilator days, ICU length of stay, APACHE and SOFA score were statistically significant as compared to non ARDS scrub typhus group.

The clinical features of scrub typhus patients at the time admission have been shown in Table 3. The most common clinical feature in both groups were fever, headache, nausea, vomiting, myalgia, generalized weakness, pain abdomen, chest pain, conjunctival congestion, hepato-splenomegaly, eschar and macula-papular rashes. The clinical feature such as dyspnea, cough, low blood pressure (mean arterial pressure <65 mmHg), and inferior vena cava collapsibility of $>50\%$ by ultrasound (hypovolemia) were statistically significant in scrub typhus patients with ARDS.

Table 4 shows the initial laboratory parameters of scrub typhus patients at the time admission. The laboratory parameters such as decreased hemoglobin, hematocrit, serum albumin, and increased serum creatinine, serum total bilirubin, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, lactate dehydrogenase (LDH), creatine phosphokinase (CPK), and serum lactate were statistically significant ($P < 0.0001$) in scrub typhus patients group with ARDS.

Table 1: The clinical characteristics of scrub typhus patients with or without ARDS

Clinical characteristics	Mean±SD (%)		P
	Scrub typhus patients without ARDS (n=34)	Scrub typhus patients with ARDS (n=24)	
Age in years	49.44±2.55	52.50±3.72	0.486
Sex	Males-16/females-18	Males-19/females-5	
Comorbidities	CVA: 1	CVA: 2	
	Hypertension: 9	Hypertension: 6	
	CAD: 2	CAD: 2	
	CKD: 2	CKD: 1	
	DM: 8	DM: 6	
	Asthma: 1	Asthma: 1	
	Hypothyroidism: 1	Hypothyroidism: 1	
	COPD: 2	COPD: 0	
	No comorbidities: 15	No comorbidities: 10	
	Patients from endemic area	24/34 (70.5)	20/24 (83.3)
Complications	AKI: 2/34 (5.8)	AKI: 18/24 (75)	<0.0001
	Acute liver failure: 3/34 (8.8)	Acute liver failure: 14/24 (58.3)	<0.0001
	Upper GI bleed: 2/34 (5.8)	Upper GI bleed: 4/24 (16.65)	0.190
	VAP: 1/34 (2.9)	VAP: 0/24	0.406
	CRBSI: 1/34 (2.9)	CRBSI: 1/24 (4.1)	0.805
	UTI: 1/34 (2.9)	UTI: 2/24 (8.35)	0.805
	Seizures: 0/34	Seizures: 1/24 (4.1)	0.237
Days of fever before doxycycline started	5.264±0.431	11.333±0.570	<0.0001

CVA: Cerebrovascular accident, CAD: Coronary artery disease, CKD: Chronic kidney disease, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, AKI: Acute kidney injury, VAP: Ventilator-associated pneumonia, CRBSI: Catheter-related blood stream infections, UTI: Urinary tract infection, SD: Standard deviation, ARDS: Acute respiratory distress syndrome

Table 2: PaO₂/FiO₂ ratio and LIS with mortality

	Mean±SD		P
	Scrub typhus patients without ARDS (n=34)	Scrub typhus patients with ARDS (n=24)	
PaO ₂ /FiO ₂ ratio (PFR)	310.411±40.628	169.916±59.644	<0.0001
LIS	1.352±0.793	3.479±1.220	<0.0001
Number of patients intubated	11.764±0.056	91.666±0.057	<0.0001
Number of ventilator days	2.25±0.27	4.50±0.43	0.001
ICU length of stay	4.02±0.28	7.08±0.43	<0.0001
28 days mortality	0.00±0.00	8.333±0.058	0.09
APACHE score	8.794±0.545	16.083±1.173	<0.0001
SOFA score	5.235±0.216	9.00±0.735	<0.0001

LIS: Lung injury score, ICU: Intensive Care Unit, APACHE: Acute Physiology and Chronic Health Evaluation, SOFA: Sequential Organ Failure Assessment, SD: Standard deviation, ARDS: Acute respiratory distress syndrome

The correlation between WF and ICT of scrub typhus patients at the time admission have been shown in Table 5. In our observational study all patients were positive for scrub typhus by ICT but WF titers were insignificant (<1:80) in 7 of them.

Discussion

Scrub typhus is a mite borne acute infectious disease caused by *O. tsutsugamushi*. *O. tsutsugamushi* is an obligate intracellular Gram-negative bacterium. Mites are both the vectors and the reservoirs.^[9] Humans are accidental hosts. It affects people of all ages. The mortality of scrub typhus in untreated patients range from 0% to 30% and tends to vary with age and region of infection. Generally seen in people whose occupational or recreational activities bring them into contact with ecotypes favorable with vector chiggers.^[10]

Scrub typhus manifest as either nonspecific febrile illness or multi-organ dysfunction such as AKI, ARDS, myocarditis, hepatitis, and meningo-encephalitis. In our prospective observational study conducted over 12 months, 58 patients had scrub typhus. Table 1 shows the clinical characteristics of scrub typhus patients with or without ARDS. The involvement of lungs has been described which range from bronchitis and interstitial pneumonitis to ARDS.^[11] Figure 1 shows chest X-ray of scrub patient with severe ARDS. The pathogenesis of ARDS in scrub typhus is not known, thought to be immunological response of the lung to previous *O. tsutsugamushi* infection without direct invasion of the organism and diffuse alveolar damage without evidence of vasculitis.^[12] High incidence of ARDS (24 patients) has been observed in our study. When the patients presented with atypical symptoms, initially they were not diagnosed (delay in diagnosis) as scrub typhus at outside hospital or when the patient came to our hospital it was average 11.333 ± 0.570 days and 5.264 ± 0.431 days from the onset of signs and symptoms in scrub typhus patients with and without ARDS, respectively. Probably delay in treatment might have caused a high incidence of ARDS.

Table 2 shows PaO₂/FiO₂ ratio, ICU length of stay and mortality. The majority of patients in ARDS group had moderate ARDS, the number of ventilator days and ICU mortality were high which was statistically significant ($P < 0.05$). Eschar is a vesicular lesion at the site of mite feeding is the first sign of disease and also pathognomonic of scrub typhus often found in the groin, axilla, genitalia, and neck. This is rarely seen in South East Asia and Indian subcontinent.^[13-15] In our

observational study, 6 out of 34 scrub patients without ARDS and 4 out of 24 scrub patients with ARDS had Eschar. Figure 2 shows the Eschar seen near right axilla in one of our patient coming from an endemic area.

Table 3 shows the clinical features of scrub typhus patients with or without ARDS. Fever, headache,

Table 3: The clinical features of scrub typhus patients with or without ARDS

Symptoms and signs	Scrub typhus patients without ARDS (n=34) (%)	Scrub typhus patients with ARDS (n=24) (%)	P
	Fever	32 (94.1)	
Headache	22 (67.6)	20 (83.3)	0.185
Nausea/vomiting	22 (67.6)	8 (33.3)	0.009
Myalgia	18 (52.9)	18 (75)	0.091
Generalized weakness	14 (41.1)	18 (75)	0.010
Cough	9 (26.4)	24 (100)	<0.0001
Dyspnea	4 (11.7)	21 (87.5)	<0.0001
Pain abdomen	20 (58.8)	7 (29.1)	0.026
Chest pain	3 (8.8)	1 (4.1)	0.680
Conjunctival congestion	22 (67.6)	22 (91.6)	0.031
Altered sensorium	1 (2.9)	2 (8.3)	0.370
MAP <65 mmHg	7 (20.5)	17 (70.8)	<0.0001
Hepatomegaly	12 (35.2)	6 (25)	0.413
Splenomegaly	2 (5.8)	2 (8.3)	0.723
Eschar	6 (17.6)	4 (16.6)	0.924
Maculopapular rash	4 (11.7)	6 (25)	0.195
IVC collapsibility	15 (44.1)	22 (91.6)	<0.0001

IVC: Inferior vena cava, MAP: Mean arterial pressure, ARDS: Acute respiratory distress syndrome

Table 4: The laboratory parameters (at admission) of scrub typhus patients with or without ARDS

Laboratory parameters (at admission)	Mean±SD		P
	Scrub typhus patients without ARDS (n=34)	SCRUB typhus patients with ARDS (n=24)	
Hemoglobin	13.293±0.244	9.576±0.267	<0.0001
Hematocrit	39.879±0.743	34.221±0.922	<0.0001
WBC	6913.2±410.4	11429.1±444.1	<0.0001
Platelets	86755.8±4812.8	74250.0±6766.6	0.127
Na (sodium)	132.14±0.988	136.37±1.459	0.016
K (potassium)	4.306±0.153	4.308±0.176	0.992
Cl (chloride)	98.412±1.467	99.083±1.545	0.759
Serum creatinine	1.063±0.043	2.629±0.271	<0.0001
PT	15.497±0.278	16.542±0.763	0.152
INR	1.436±0.040	1.492±0.072	0.471
APTT	31.279±0.527	32.750±1.397	0.272
Total bilirubin	1.130±0.064	2.883±0.339	<0.0001
SGOT (AST)	56.000±1.842	150.87±29.83	<0.0001
SGPT (ALT)	59.147±1.885	112.917±10.58	<0.0001
Serum albumin	3.397±0.072	2.212±0.156	<0.0001
Serum lactate	12.706±0.633	25.546±2.386	<0.0001
LDH	520.588±46.93	3790.33±701.1	<0.0001
CPK	321.41±32.725	565.66±58.877	<0.0001

WBC: White blood cell, LDH: Lactate dehydrogenase, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, CPK: Creatine phosphokinase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, PT: Partial thromboplastin, APTT: Activated partial thromboplastin time, INR: International normalized ratio, SD: Standard deviation, ARDS: Acute respiratory distress syndrome

conjunctival congestion, myalgia, generalized weakness, vomiting, and pain abdomen were the common clinical features. In ARDS group, the hypovolemia was more common which was statistically significant ($P < 0.05$). Table 4 shows the laboratory parameters (at admission) of scrub typhus patients with or without ARDS. Patients in ARDS group had more severe disease in the form of deranged liver parameters, increased serum creatinine, elevated LDH, CPK, and serum lactate.

Serology is the mainstay of diagnosing scrub typhus, immuno-florescence antibody test or indirect immuno-peroxidase assay is the gold standard.^[16] Due to high-cost factor and nonavailability of above two tests we have done both ICT and WFT in all 109 patients. Based on either ICT/WFT positivity patients we considered as scrub typhus positive. 51 patients were excluded as they were negative for both ICT/WFT. Remaining 58 patients were positive for interstitial cystitis test whereas 7 patients who are positive for ICT had WF titer <1:80. This shows that the WFT, which is cheap and commonly used in resource limited countries,^[17-19] has a sensitivity of 30% and specificity of 100% at titer breakpoint of 1:80 in detection of scrub typhus.^[20] ICT has a sensitivity of 39.1% and specificity 99.5%.^[21] WFT results among patients of immuno-chromatography proven scrub typhus with or without ARDS have been shown in Table 5. The patients in ARDS group had high WF titers (1:320). The higher titers of WF can be correlated with more severe form of the disease according to our observation.^[22,23]

Doxycycline has been considered as a drug of choice for treatment of scrub typhus. The optimal duration of therapy is uncertain. Short courses of doxycycline or chloramphenicol are associated with an

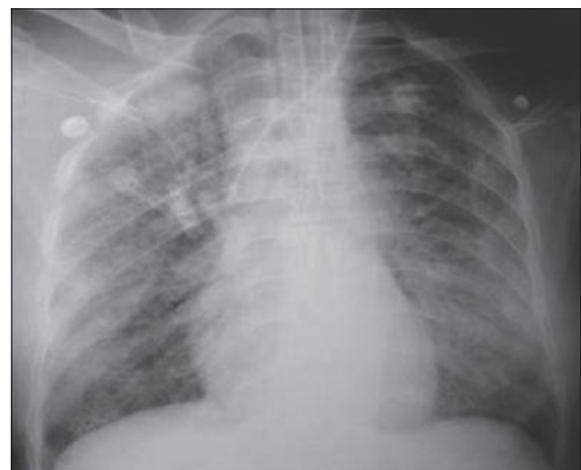


Figure 1: Chest X-ray showing acute respiratory distress syndrome in patient with scrub typhus

Table 5: WFT results among patients of immuno-chromatography proven scrub typhus with or without ARDS

WFT (n=58)	Scrub typhus patients without ARDS (n=34)	Scrub typhus patients with ARDS (n=24)
1:20	02	-
1:40	05	-
1:80	20	08
1:160	03	06
1:320	04	10
Total (n=58)	34	24

ARDS: Acute respiratory distress syndrome, WFT: Weil-Felix test

increased risk of relapse.^[24] Treatment of scrub typhus was initiated with doxycycline in 56 patients and combination of doxycycline and azithromycin was used in 2 patients with ARDS and multiple organ dysfunction syndrome (MODS). All the 58 patients were treated for 10 days. Most of the patients responded to doxycycline therapy within 2–3 days except 2 patients who died due to severe MODS (four organ involvement) and they were referred fairly late to our hospital. Azithromycin has shown to have comparable efficacy when compared to doxycycline in a small trial.^[25] Rifampicin can be used in combination with azithromycin or doxycycline in cases of poor response to doxycycline alone.^[26] All 34 scrub typhus patients without ARDS recovered completely and discharged. Among 24 scrub typhus patients with ARDS, 22 patients recovered, and 2 patients died (Refractory septic sepsis with severe MODS).

Conclusion

Scrub typhus is an important differential diagnosis in patients having fever with thrombocytopenia. Scrub typhus with ARDS has high morbidity and mortality. Early diagnosis using ICT in a patient from the rural background with a history of fever, thrombocytopenia and multiorgan dysfunction and treatment with doxycycline in these patients can help to reduce mortality.

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References

- Tamura A, Ohashi N, Urakami H, Miyamura S. Classification of Rickettsia tsutsugamushi in a new genus, Orientia gen. nov. as *Orientia tsutsugamushi* comb. nov. *Int J Syst Bacteriol* 1995;45:589-91.
- Chogle AR. Diagnosis and treatment of scrub typhus – The Indian scenario. *J Assoc Physicians India* 2010;58:11-2.
- Watt G, Parola P. Scrub typhus and tropical rickettsioses. *Curr Opin Infect Dis* 2003;16:429-36.
- Kothari VM, Karnad DR, Bichile LS. Tropical infections in the ICU. *J Assoc Physicians India* 2006;54:291-8.



Figure 2: Eschar over anterior chest wall near axilla - on right side

- Mahajan SK. Scrub typhus. *J Assoc Physicians India* 2005;53:954-8.
- Wang CC, Liu SF, Liu JW, Chung YH, Su MC, Lin MC. Acute respiratory distress syndrome in scrub typhus. *Am J Trop Med Hyg* 2007;76:1148-52.
- Subbalaxmi MV, Murali Krishna M, Krishna Prasad A, Teja VD, Swaroopa K, Chandra N, *et al.* Outbreak of scrub typhus in Andhra Pradesh – Experience at a tertiary care hospital. *J Assoc Physicians India* 2014;60:490-6.
- ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, *et al.* Acute respiratory distress syndrome: The Berlin definition. *JAMA* 2012;307:2526-33.
- Lerdthusnee K, Khuntirat B, Leepitakrat W, Tanskul P, Monkanna T, Khlaimanee N, *et al.* Scrub typhus: Vector competence of *Leptotrombidium* chiangraiensis chiggers and transmission efficacy and isolation of *Orientia tsutsugamushi*. *Ann N Y Acad Sci* 2003;990:25-35.
- Walker JS, Chan CT, Manikumar C, Elisberg BL. Attempts to infect and demonstrate transovarial transmission of *R. tsutsugamushi* in three species of *Leptotrombidium* mites. *Ann N Y Acad Sci* 1975;266:80-90.
- Chayakul P, Panich V, Silpapojakul K. Scrub typhus pneumonitis: An entity which is frequently missed. *Q J Med* 1988;68:595-602.
- Park JS, Jee YK, Lee KY, Kim KY, Myong NH, Seo PW. Acute respiratory distress syndrome associated with scrub typhus: Diffuse alveolar damage without pulmonary vasculitis. *J Korean Med Sci* 2000;15:343-5.
- Varghese GM, Abraham OC, Mathai D, Thomas K, Aaron R, Kavitha ML, *et al.* Scrub typhus among hospitalised patients with febrile illness in South India: Magnitude and clinical predictors. *J Infect* 2006;52:56-60.
- Vivekanandan M, Mani A, Priya YS, Singh AP, Jayakumar S, Purty S. Outbreak of scrub typhus in Pondicherry. *J Assoc Physicians India* 2010;58:24-8.
- Sharma A, Mahajan S, Gupta ML, Kanga A, Sharma V. Investigation of an outbreak of scrub typhus in the himalayan region of India. *Jpn J Infect Dis* 2005;58:208-10.
- Koh GC, Maude RJ, Paris DH, Newton PN, Blacksell SD. Diagnosis of scrub typhus. *Am J Trop Med Hyg* 2010;82:368-70.
- Mathai E, Lloyd G, Cherian T, Abraham OC, Cherian AM. Serological evidence for the continued presence of human rickettsioses in southern India. *Ann Trop Med Parasitol* 2001;95:395-8.
- Kamarasu K, Malathi M, Rajagopal V, Subramani K, Jagadeeshramasamy D, Mathai E. Serological evidence for wide distribution of spotted fevers and typhus fever in Tamil Nadu. *Indian J Med Res* 2007;126:128-30.
- Mahajan SK, Rolain JM, Sankhyan N, Kaushal RK, Raoult D. Pediatric scrub typhus in Indian Himalayas. *Indian J Pediatr* 2008;75:947-9.
- Mahajan SK, Kaushik M, Raina R. Relevance of Weil-Felix test in diagnosis of scrub typhus in India. *J Assoc Physicians India* 2006;54:619-21.
- Blacksell SD, Jenjaroen K, Phetsouvanh R, Tangamuehitcharnchai A, Phouminh P, Phongmany S, *et al.* Accuracy of rapid IgM-based

- immunochromatographic and immunoblot assays for diagnosis of acute scrub typhus and murine typhus infections in Laos. *Am J Trop Med Hyg* 2010;83:365-9.
22. Sonthayanon P, Chierakul W, Wuthiekanun V, Phimda K, Pukrittayakamee S, Day NP, *et al.* Association of high *Orientia tsutsugamushi* DNA loads with disease of greater severity in adults with scrub typhus. *J Clin Microbiol* 2009;47:430-4.
23. Kim DM, Kang DW, Kim JO, Chung JH, Kim HL, Park CY, *et al.* Acute renal failure due to acute tubular necrosis caused by direct invasion of *Orientia tsutsugamushi*. *J Clin Microbiol* 2008;46:1548-50.
24. Sheehy TW, Hazlett D, Turk RE. Scrub typhus. A comparison of chloramphenicol and tetracycline in its treatment. *Arch Intern Med* 1973;132:77-80.
25. Phimda K, Hoontrakul S, Suttinont C, Chareonwat S, Losuwanaluk K, Chueasuwanchai S, *et al.* Doxycycline versus azithromycin for treatment of leptospirosis and scrub typhus. *Antimicrob Agents Chemother* 2007;51:3259-63.
26. Watt G, Chouriyagune C, Ruangweerayud R, Watcharapichat P, Phulsuksombati D, Jongsakul K, *et al.* Scrub typhus infections poorly responsive to antibiotics in northern Thailand. *Lancet* 1996;348:86-9.

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