ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 05 | May - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# COMPLICATIONS IN SCRUB TYPHUS: A CASE SERIES FROM TERTIARY CARE HOSPITAL

General Medicine

**Dr Pooja Baradia** Senior Resident, Dept. of Medicine, Gandhi Medical College & Hamidia Hospital Bhopal.

**Dr Ashutosh Kumar** Professor, Dept. of Medicine, LN Medical College & Research center.

**Dr Ishan Verma** Assistant Professor, Dept. of Medicine, AIIMS Nagpur.

**Dr Rishabh Dodeja*** PG Resident, Dept. of Medicine, LN Medical College & Research center. *Corresponding Author

**Dr Narmada Patel** Professor, Dept. of Medicine, LN Medical College & Research center.

**Dr Apurva Khare** Professor, Dept. of Medicine, LN Medical College & Research center.

## ABSTRACT

Scrub typhus is the most common re-emerging Rickettsia infection in India and many other South East Asian countries. The first sign of scrub typhus disease in patients is a vesicular lesion called eschar. Serious complications in the form of myocarditis, pneumonia, meningoencephalitis, acute renal failure, and gastrointestinal bleeding may occur. It is an acute febrile illness which has significant morbidity and mortality. In patients with fever during monsoon months, a high index of suspicion for scrub should be kept. We are presenting a case series with varied presentation and complications in patients with scrub typhus for better understanding of this disease.

## KEYWORDS

Fever, Tsutsugamushi, Typhus, Scrub

## INTRODUCTION:

Scrub typhus is caused by *Orientia tsutsugamushi* (formerly *Rickettsia*) and it is transmitted to humans by vector of the *Trombiculidae* family (*Leptotrombidium deliense* and *L. akamushi*).[1]

The infection transmission is through the larval mites or "chiggers."[2] The incubation period of *O. tsutsugamushi* in humans is around 10–12 days. Patients usually present with pyrexia of unknown origin (PUO)[3]

The first sign of scrub typhus is usually a vesicular lesion at the site of mite feeding, called an eschar. It typically presents with black necrotic center and an erythematous border at the site of the chigger bite and is often found in the groin, axilla, genitalia, and neck. The prevalence of eschar in patients of scrub typhus ranges from 7% to 80%. It is an important clue for diagnosis and is a pathognomonic sign.[1]

The most common complaint is fever which starts abruptly and is associated with severe headache, drowsiness, lymphadenopathy and hepatosplenomegaly. After 1 week, a maculopapular rash starts appearing from the trunk and spreads to the limbs.

By the end of the 2nd week, systemic symptoms begin mostly involving the central nervous system, cardiovascular, renal, respiratory, or gastrointestinal systems. Serious complication may occur in the form of myocarditis, pneumonia, meningoencephalitis, acute renal failure, and gastrointestinal bleeding. Patients of scrub typhus who have higher white blood cell (WBC) counts, lower hematocrit, higher bilirubin levels, and delayed treatment with anti-bacterial drugs have higher chances of developing respiratory distress.[1]

Serology is the mainstay of diagnosis. In primary infection with *O. tsutsugamushi*, the antibody titer at the end of the 1st week is significant, which are mainly IgM antibodies, IgG antibodies appear at the end of the 2nd week.[4]

Tetracycline or chloramphenicol are the mainstay of therapy in patients in whom scrub typhus is suspected. The other antibacterial which are found to be effective are azithromycin, rifampicin and roxithromycin.[5]

We are presenting a case series with varied presentation and complications for better understanding of this disease.

## MATERIAL AND METHODS:

This is a case series of 7 patients diagnosed of scrub typhus. Demographic details, comorbidities, clinical features, treatment were noted down after obtaining consent from the patients.

## RESULTS:

### Case 1:

A 20-year-old male, came to OPD in drowsy state. Patient had high grade fever for past ten days, and vomiting for 2 days. There was history of recurrent generalized tonic-clonic seizure episodes.

Vitals on admission: PR - 106/min, BP - 120/70 mmHg, SpO2 - 95% (room air)

Patient was febrile, semi- comatose, pupils sluggishly reactive to light with neck stiffness. Patient had eschar marks on back, right hand finger and scrotum. (Figure 1-3) Cardiac and respiratory examination was within normal limits.

Figure1: Eschar Mark on finger.

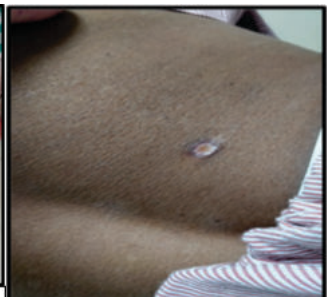

Figure 2: Eschar Mark on back.

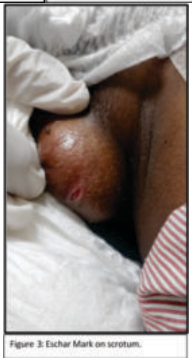

Figure 3: Eschar Mark on scrotum.

**Laboratory Investigations:**
Hemoglobin 13 g/dl, Total leucocyte count 8600/mm$^3$, and platelets 2.40 lac/mm$^3$. RFT and LFT were within normal limits. CSF analysis was done, colorless, glucose 72mg/dl, protein 32.5 mg/dl, WBC 5 cells/cumm, adenosine deaminase (ADA) 0.4 U/L. CSF culture was sterile. Blood culture sterile, urine culture- candida albicans. Malaria parasite negative. Scrub typhus IGM ELISA was positive.

Imaging: MRI Brain revealed no abnormality. EEG revealed diffuse cerebral dysfunction with interictal epileptiform discharges.

Symptomatic supportive treatment was given. Diagnosis of scrub typhus with acute febrile encephalopathy was made and patient was put on parenteral Doxycycline 100mg BD, Azithromycin 500 mg OD. Patient showed signs of improvement, gained consciousness and was discharged on the 21$^{st}$ day.

**Case 2:** A 54-year-old man, came to emergency with complains of fever, generalized weakness and breathlessness for 10 days.

Vitals on admission: PR - 90/min, BP - 130/80 mmHg, SpO2 - 82% on room air

He was febrile and conscious. Bilateral coarse crepitations were present. CVS and per abdomen findings were within normal limits. An eschar mark was found on abdomen. (Figure 4)

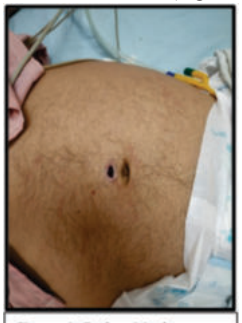

Figure 4: Eschar Mark on abdomen

Laboratory investigations: Complete blood count- Hemoglobin 9.5 g/dl, Total leucocyte count 9500/mm$^3$, and platelets 45000/mm$^3$ Serum sodium 130 mmol/l, potassium 4 mmol/l. Blood urea was 37 mg/dl and serum creatinine 1.46 mg/dl. The liver function tests total bilirubin 2.9 mg/dl, SGOT 88 U/L SGPT 100U/L, Albumin 1.8 g/dl. Blood gas analysis showed pH-7.44, pCO2-25.2, pO2-93, HCO3- 16.9 Dengue serology and malarial antigen came negative. Scrub typhus IGM was positive with titer of 4.68. Leptospira IGM was negative.

Imaging: Chest X ray s/o left lung collapse (Figure 5-6)

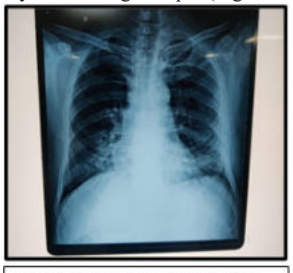

Figure 5: Chest x ray on admission

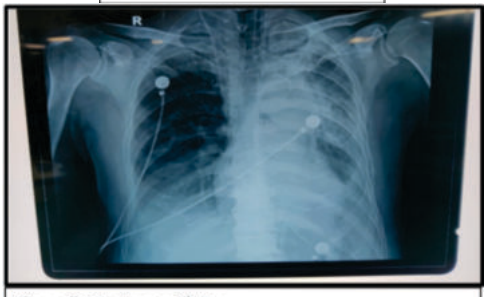


Figure 6: Chest x ray 8$^{th}$ day

HRCT Chest revealed multiple ground glass patches with interstitial septal thickening in both lung fields, mild pleural effusion on both sides, findings were suggestive of pulmonary edema (CORADS 3).

Patient was put on symptomatic and supportive treatment. He was put on oxygen support. Injection doxycycline, Tablet Azithromycin was given. Albumin was replaced. Patient had continuous febrile episodes often with dip in saturation levels.

COVID RTPCR was negative. D Dimer was raised 1000 ng/ml and LDH was 553 U/L. He was put on non-invasive ventilator (CPAP). Patient continued to worsen, he developed respiratory failure and was intubated and put on mechanical ventilation. Patient's condition continued to deteriorate, he developed multiple organ dysfunction and sepsis and had sudden cardiac arrest.

**Case 3**: A 19-year-old man came with complains of fever and mild cough for 4 days in medicine OPD.

Vitals on admission: PR - 70/min, BP - 100/70 mmHg, SpO2 - 97% (room air)

Patient was febrile, systemic examination was normal. No eschar mark was present. Laboratory investigations are shown in table 1. Scrub typhus IGM was positive.

Oral doxycycline and Azithromycin were started. Patient had a fast recovery and was discharged after 1 week.

**Case 4:** A 50-year-old man came with complaints of fever and cough with sputum for 7 days. He was a chronic smoker with no comorbidities.

Vitals on admission: PR - 76/min, BP - 110/60 mmHg, SpO2 - 95% room air

On examination, bilateral basal crepitations were present in chest. Eschar mark was found on back of thigh of patient. (Figure 7)

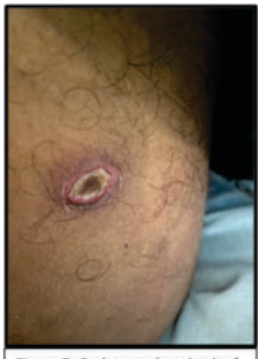

Figure 7: Eschar mark on back of thigh

Laboratory investigations: presented in table 1.

CKMB and TROP I was negative. ECG was normal. ECHO showed mild concentric Left ventricular hypertrophy. Scrub typhus IGM was positive.

Imaging: HRCT Chest revealed mild bilateral pleural effusion, atelectatic opacities in right lower lobe mild pericardial effusion. USG revealed mild hepatosplenomegaly.

Oral Doxycycline and Azithromycin were started. Patient showed signs of derangement of renal function, had acute kidney injury. But patient showed recovery and was discharged after 1 week.

**Case 5:** A 17-year-old female, presented to the hospital with complaints of high-grade fever, headache and myalgia for 5 days. She had reactive antibody for Scrub Typhus. On the second day of admission, she developed diplopia and was unable to sit and stand properly by herself.

Vitals on admission: stable, on neurological examination, she was found to have truncal ataxia and left abducens nerve palsy. No neck rigidity. (Figure 8)

**Table1:**

| Case no. | Hemoglobin (g/dl) | Total Leucocyte Count (/cumm) | Platelet (lac/cumm) | Blood Urea (mg/dl) | Serum Creatinine (mg/dl) | Sodium (Meq/L) | Potassium (Meq/L) | Total bilirubin (mg/dl) | SGOT (U/L) | SGPT (U/L) | Serum Albumin (g/dl) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 12 | 8600 | 2.4 | 9 | 0.7 | 141 | 3.2 | 1 | 91 | 112 | 2 |
| 2 | 9.5 | 9500 | 0.45 | 37 | 1.46 | 130 | 4 | 2.9 | 88 | 100 | 1.8 |
| 3 | 15.3 | 2400 | 0.8 | 24 | 1.09 | 138 | 4.1 | 0.6 | 297 | 551 | 4 |
| 4 | 11.5 | 6000 | 0.82 | 31 | 0.96 | 134 | 3.5 | 0.6 | 172 | 196 | 2.1 |
| 5 | 11 | 5400 | 1.21 | 18 | 0.88 | 136 | 3.8 | 0.7 | 80 | 112 | 2.5 |
| 6 | 13.5 | 13100 | 1.13 | 24 | 0.58 | 136 | 3.7 | 3.3 | 143 | 153 | 2.5 |
| 7 | 13.8 | 5100 | 1.68 | 40 | 0.97 | 130 | 4.3 | 0.8 | 107 | 71 | 2.4 |

**Table2:**

| Case no. | Age /Sex | Eschar | Site of Eschar | Scrub typhus IgM | Duration of illness | Outcome |
|---|---|---|---|---|---|---|
| 1 | 20/M | Present | Back, Finger, Scrotum | Positive 3.55 | 10 days | Discharged healthy |
| 2 | 54/M | Present | Abdomen | Positive 4.68 | 10 days | Died |
| 3 | 19/M | Absent | - | Positive 20.03 | 4 days | Discharged healthy |
| 4 | 50/M | Present | Back Of Thigh | Positive 2.56 | 7 days | Discharged healthy |
| 5 | 17/F | Absent | - | Positive 2.3 | 5 days | Discharged healthy |
| 6 | 35/M | Present | Chest | Positive 6.55 | 14 days | Discharged healthy |
| 7 | 45/M | Present | Chest | Positive 2.76 | 5 days | Discharged healthy |

Figure 8: Left 6th nerve palsy

Both Kernig's and Brudzinski signs were absent. Other system examination including respiratory, cardiovascular and gastrointestinal system, were normal. She had no eschar on her body.

Laboratory investigations: presented in table 1.

CSF analysis: lymphocytic pleocytosis (WBCs – 20cells/cumm, lymphocytes 60%), glucose- 39.6 mg/dl and proteins – 69 mg/dl. CSF for TB PCR was negative.

The patient was put on Doxycycline which was given for 14 days and she responded well to the treatment**.**

**Case 6:** A 35-year-old man came to medicine OPD with complains of fever and mild cough for 14 days.

Vitals on admission: PR - 86/min, BP - 100/60 mmHg, SpO2 - 96% room air

Physical examination was normal. An eschar mark was found on chest. (Figure 9)

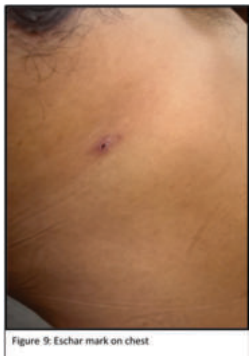

Figure 9: Eschar mark on chest

Laboratory investigations: presented in table 1. Dengue serology and malarial antigen came negative. Scrub typhus IGM was positive with titer of 6.55. Urine routine microscopy indicated mild proteinuria.

Patient was put on Oral Doxycycline and Azithromycin. Patient had a good recovery and was discharged within a week.

**Case 7:** A 45-year-old male came with complaints of fever for 5 days with breathlessness.

Vitals on admission: PR - 98/min, BP - 130/90 mmHg, SpO2 - 84% room air

On physical examination, patient was conscious oriented with bilateral basal crepitations in lungs. Eschar mark was found on chest below axilla. (Figure 10)

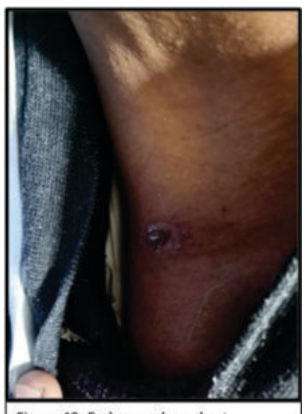

Figure 10: Eschar mark on chest

Laboratory investigations: (table 1). Dengue serology and malarial antigen came negative. Scrub typhus IgM was positive with titer of 2.76. Blood gas analysis showed, pH-7.42, pCO2-24.8, pO2-72, HCO3- 18.4

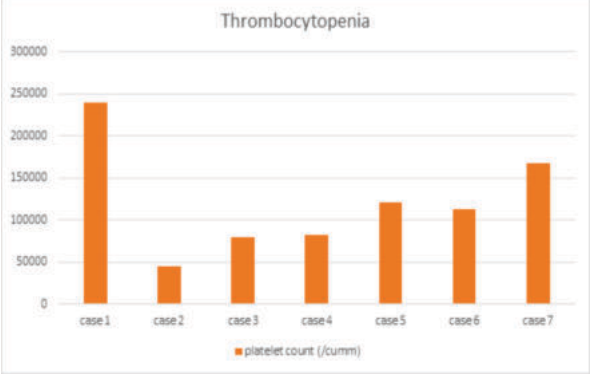


**Figure 13**

Patient was given oxygen through face mask and was put on parenteral Doxycycline and oral Azithromycin. He developed type 1 respiratory failure with lower respiratory tract infection. Patient gradually recovered and was discharged within a week.

Summary of all cases described in table 2.

Thombocytopenia was found in 4 patients. (Figure 13)

## DISCUSSION:

Fever and headache in the setting of eschar or maculo-papular rash should alert the physician regarding this diagnosis.[9,10]

Central nervous system (CNS) is the most crucial target in other rickettsia diseases.[6] In comparison, the burden of neurological complications in scrub typhus was perceived to be low. Evidence in literature suggest that *O. tsutsugamushi* invades the CSF and CNS invasion is seen only in 2%–5% cases of tsutsugamushi disease.[6,7,8] In our study we found out of seven two patients having neurological manifestations. Common CNS presentations are nuchal rigidity, seizures, delirium, and meningitis.[9,10,11]

Patients with scrub typhus with low body temperature, a rapid pulse rate, the presence of lung signs, a low percentage of lymphocytes, low serum albumin, elevated aspartate aminotransferase, elevated serum creatinine, and positive urine albumin require special attention[12]. In our study most patients had low albumin, elevated liver enzymes. Proteinuria was found in one case.

We found thrombocytopenia in four patients. Scrub typhus may cause thrombocytopenia and MODS. Previous studies have shown that thrombotic microangiopathic syndrome is the mechanism of thrombocytopenia-associated MODS.[13,14] Pathological changes such as thrombotic thrombocytopenic purpura (TTP), secondary thrombotic microangiopathy (TMA), and DIC may occur in the patients.[13] The early use of antibacterial is very important to avoid life-threatening scrub typhus[15]

We found deranged renal function tests in five patients. AKI and renal involvement in scrub typhus are believed to be multifactorial in origin. The possible mechanisms of renal failure include prerenal failure, septic shock, rhabdomyolysis, vasculitis, acute interstitial nephritis, and direct renal invasion of O. tsutsugamushi.[16] Renal involvement due to scrub typhus has not received much attention. A recent systematic review found only a few case reports specifically describing acute renal failure due to scrub typhus.[19] Overall, renal involvement is considered to be a part of the multi-organ dysfunction syndrome in patients with severe disease.[20,21] The mechanism of AKI is impaired renal perfusion due to volume depletion or increased vascular permeability.[22]

In this study three patients had respiratory manifestations and two required oxygen support. Respiratory manifestations in scrub are usually seen during the 2nd week of untreated illness and the presentation ranged from flu-like symptoms, bronchitis, interstitial pneumonitis to ARDS.[23,24] Untreated patients entering the 2nd week of illness develop serious complication such as severe respiratory distress syndrome, encephalitis, interstitial pneumonia, myocarditis, AKI, acute hepatic failure, pancreatitis, and septic shock.[25,26] These clinical manifestations are due to generalized vasculitis due to the invasion of the endothelial cell by the organism and perivascular infiltrate of leukocyte.

We encountered one case with abducens nerve palsy. Involvement of abducens nerve in scrub is usually rare, and was seen in one other study[27].

We observed that the patient who died had lowest platelet count, highest bilirubin and low albumin levels. Case number 3 had no eschar mark, but serology markers were highly positive indicating its high sensitivity.[4]

## CONCLUSION:

The diagnosis of Scrub typhus is often missed, and tools for prompt diagnosis are often not available in resource-poor setups of our country. Also delay in initiating treatment may lead to increased fatality. Through this study we want to spread awareness for early diagnosis to avoid complications. More widespread access to medical care, close suspicion of the disease along with the early use of affordable and accurate rapid tests, can improve management of this condition which can be easily treated with antibacterials.

**Acknowledgement:**

We wish to thank Dr. D. P. Singh (Professor and Head, Department of Medicine) for constantly supporting, guiding and promoting research work. Special thanks to Dr. M.K. Jain for suggesting edits and providing intellectual guidance.

## REFERENCES:

1. Chakraborty S, Sarma N. Scrub Typhus: An Emerging Threat. Indian J Dermatol. 2017 Sep-Oct;62(5):478-485. doi: 10.4103/ijd.IJD_388_17. PMID: 28979009; PMCID: PMC5618834.
2. Lai CH, Huang CK, Chen YH, Chang LL, Weng HC, Lin JN, et al. Epidemiology of acute q fever, scrub typhus, and murine typhus, and identification of their clinical characteristics compared to patients with acute febrile illness in Southern Taiwan. *J Formos Med Assoc*. 2009;108:367–76.
3. 11. Saah AJ. *Orientia tsutsugamushi* (scrub typhus) In: Mandell GL, Bennett JE, Dolin R, editors. *Principles and Practice of Infectious Disease*. 5th ed. Philadelphia, Pa: Churchill Livingstone; 2000. pp. 2056–7.
4. Koh GC, Maude RJ, Paris DH, Newton PN, Blacksell SD. Diagnosis of scrub typhus. Am J Trop Med Hyg. 2010 Mar;82(3):368-70. doi: 10.4269/ajtmh.2010.09-0233. PMID: 20207857; PMCID: PMC2829893.
5. Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. Harrison's principles of internal medicine, 19e. New York, NY, USA:: Mcgraw-hill; 2015.
6. Sood AK, Chauhan L, Gupta H. CNS manifestations in *Orientia tsutsugamushi* disease (Scrub Typhus) in North India. Indian J Pediatr 2016;83:634-9.
7. Silpapojakul K, Ukkachoke C, Krisanapan S, Silpapojakul K. Rickettsial meningitis and encephalitis. Arch Intern Med 1991;151:1753-7.
8. Singh AK, Kumar A, Dhole TN. Recent trends and changing aetiology of acute encephalitis syndrome in India. Asian J Res Infect Dis 2020;3:33-47.
9. Rana A, Mahajan SK, Sharma A, Sharma S, Verma BS, Sharma A. Neurological manifestations of scrub typhus in adults. Trop Doct 2017;47:22-5.
10. Kamath V, Ganguly S, Bhatia JK. Rickettsial infections: Spreading beyond boundaries. In: Narsimalu G, editor. Progress in Medicine. Vol. 29. Mumbai: Jaypee; 2019. p. 195-9.
11. Drevets DA, Leenen PJ, Greenfield RA. Invasion of the central nervous system by intracellular bacteria. In: Clinical Microbiology Reviews. Vol.17. Oklahoma: American Society for Microbiology (ASM); 2004. p.323-47.
12. Kingston HW, Blacksell SD, Tanganuchitcharnchai A, Laongnualpanich A, Basnyat B, Day NP, Paris DH. Comparative accuracy of the InBios scrub typhus detect IgM rapid test for the detection of IgM antibodies by using conventional serology. Clin Vaccine Immunol. 2015;22(10):1130–2
13. Jamil MD, Hussain M, Lyngdoh M, Sharma S, Barman B, Bhattacharya PK. Scrub typhus meningoencephalitis, a diagnostic challenge for clinicians: a hospital based study from North-East India. J Neurosci Rural Pract. 2015;6(4):488–93.
14. Sharma SR, Masaraf H, Lynrah KG, Lyngdoh M. Tsutsugamushi disease (scrub typhus) meningoencephalitis in north eastern India: a prospective study. Ann Med Health Sci Res. 2015;5(3):163–7
15. 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(6):1148-52.
16. Xu G, Walker DH, Jupiter D, Melby PC, Arcari CM. A review of the global epidemiology of scrub typhus. PLoS Negl Trop Dis 2017;11:e0006062.
17. Lee S, Kang KP, Kim W, Kang SK, Lee HB, Park SK. A case of acute renal failure, rhabdo-myolysis and disseminated intravascular coagulation associated with scrub typhus. Clin Nephrol 2003;60:59-61.
18. Kim DM, Kang DW, Kim JO, et al. Acute renal failure due to acute tubular necrosis caused by direct invasion of *Orientia tsutsugamushi*. J Clin Microbiol 2008;46: 1548-50.
19. Rajapakse S, Rodrigo C, Fernando D (2012) Scrub typhus: pathophysiology, clinical manifestations and prognosis. Asian Pac J Trop Med 5: 261–264.
20. Raoult D (2009) Orientia tsutsugamushi (Scrub Typhus). In: Mandell GL, Bennett JE, Dolin R, editors. Mandell: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. Seventh ed: Churchill Livingstone, An Imprint of Elsevier. pp. 2529–2530
21. Reller ME, Dumler JS (2011) Scrub Typhus (Orientia tsutsugamushi). In: Kliegman RM, Stanton BF, GemeIII JWS, Schor NF, Behrman RE, editors. Kliegman: Nelson Textbook of Pediatrics. Nineteenth ed: Saunders, An Imprint of Elsevier. pp. 1045–1046.
22. Kim DM, Kang DW, Kim JO, Chung JH, Kim HL, et al. (2008) Acute renal failure due to acute tubular necrosis caused by direct invasion of Orientia tsutsugamushi. Journal of clinical microbiology 46: 1548–1550.
23. Lee JH, Lee JH, Chung KM, Kim ES, Kwak YG, Moon C, et al. Dynamics of clinical symptoms in patients with scrub typhus. Jpn J Infect Dis. 2013;66:155–7.
24. Kim DM, Kim SW, Choi SH, Yun NR. Clinical and laboratory findings associated with severe scrub typhus. BMC Infect Dis. 2010;10:10
25. Misra UK, Kalita J, Mani VE. Neurological manifestations of scrub typhus. J Neurol Neurosurg Psychiatry. 2015;86:761–6.
26. Goswami D, Hing A, Das A, Lyngdoh M. Scrub typhus complicated by acute respiratory distress syndrome and acute liver failure: A case report from Northeast India. Int J Infect Dis. 2013;17:e644–5.
27. Lee YH, Yun YJ, Jeong SH. Isolated abducens nerve palsy in a patient with scrub typhus. *J Aapos*. 2010;14:460–461. doi: 10.1016/j.jaapos.2010.06.016.