

SCRUB TYPHUS - A SERIOUSLY NEGLECTED LIFE-THREATENING DISEASE

Nagendra Chaudhary¹

Associate professor, Department of Pediatrics
Universal College of Medical Sciences
Bhairahawa, Nepal

Scrub typhus, an important cause of tropical fever in rural Asia, northern Australia, and the western Pacific islands has emerged as an important cause of pyrexia of unknown origin causing serious public health concern. Globally, more than one billion people are under threat and about one million people are affected by scrub typhus.¹ The disease is caused by a zoonotic, obligate, intracellular, gram negative bacteria (*Orientia tsutsugamushi*) transmitted by a bite of trombiculid mite (an arthropod).²

Scrub typhus in Nepal was first ever reported in 1981 and a hospital based study was done in 2004.³ In 2017, a study was conducted in National Public health laboratory (NPHL), Nepal established scrub typhus as an emerging neglected disease in the nation.⁴ The disease is grossly under-diagnosed and under-reported in low and middle income countries (LMICs) as the presentation and index of suspicion is low among clinicians. Limited awareness about the disease and lack of diagnostic facilities in developing nations like Nepal are also important reasons for the under-diagnosis of the disease and delay in specific treatment leading to increased case fatality rates.⁵ Outdoor workers, especially field workers in rural areas, have a higher risk of acquiring the disease. Tropical weather with high temperature and high humidity provides a favourable condition for mite activity and transmission of the disease.⁶

The clinical manifestations in scrub typhus are nonspecific and have wide variations in presentation. Initially, patients present with fever, rash, nausea, vomiting, headache, eschar at the bite site, myalgia, cough, generalized lymphadenopathy, and abdominal pain. Fever and headache are considered as most common clinical presentation.⁷ An ulcerated black coloured crusted lesion also known as eschar provides an important clue for the diagnosis of scrub typhus which varies from 1-97% depending on various geographical regions and studies.^{8,9} Scrub typhus should be considered as an important differential of pyrexia of unknown origin in tropical regions. If neglected and remain untreated, can lead to increased fatality rate due to various complications. The patient can have liver failure, acute kidney injury, pneumonitis, acute respiratory distress syndrome, myocarditis, septic shock, meningococcal meningitis, pericarditis, and disseminated intravascular

coagulation (DIC).^{10, 11} The case fatality rate ranges from 30-70% when no treatment measures are considered. The median case fatality rate for untreated patients is 6% and for treated patient is 1.4%. Thus, patients with acute febrile illness should be investigated for scrub typhus with high priority. Also, development of effective measures to treat, control and prevent the disease is a critical public health issue.^{12,13}

Scrub typhus presents as a flu-like febrile illness similar to many other diseases, which makes the clinical diagnosis quite difficult. Presence of an eschar and history of travel to or residence in an endemic area favours the diagnosis but eschar may not be present in all confirmed cases. Various cutaneous lesions due to spider bites, leishmaniasis, spotted fever rickettsiosis and anthrax may be similar to an eschar and produce a diagnostic dilemma. Scrub typhus can easily be misdiagnosed as malaria, dengue, leptospirosis and meningococcal disease. Laboratory studies in scrub typhus usually reveal leukopenia, thrombocytopenia, deranged hepatic and renal function, proteinuria and reticulonodular infiltrate. Clinically suspected cases can be confirmed by indirect immuno fluorescent assay (IFA), serological tests (ELISA), Weil-Felix agglutination test and polymerase chain reaction (PCR). This necessitates the urgent need of affordable and reliable diagnostic tests at all levels of health care systems in developing countries like Nepal.

A therapeutic trial of tetracycline or chloramphenicol is indicated in patients in whom the diagnosis of scrub typhus is suspected. Defervescence should occur within 24 hours of treatment. The recommended treatment regimen for scrub typhus is doxycycline (2.2 mg/kg/dose twice daily orally, maximum 200 mg/day for 7-15 days). For prophylaxis, 200 mg may be taken as a single dose. Azithromycin can be used as an alternative regimen.¹⁴ Insect repellents and use of protective clothing impregnated with benzyl benzoate can be used as an important preventive measure which avoids chigger bites preventing *O. tsutsugamushi*. Application of diethyltoluamide preparations to socks also helps in preventing chigger bites.¹⁵

Infection provides immunity to reinfection by homologous but not heterologous strains; however, since natural strains are highly heterogeneous, infection does not always provide

complete protection against reinfection.¹⁴

Vaccines were developed and tested, however, no single antigen has been identified that induces protection against all of the antigenically diverse strains of *O. tsutsugamushi*. Hence, early diagnosis and treatment are imperative to reduce the mortality and the complications associated with the disease. Even though scrub typhus can be a life-threatening disease, collaborative actions in the countries and regions in the endemic areas using appropriate strategies can effectively control and prevent the outbreak of this neglected disease.

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