

Scrub Typhus – An Emerging Public Health Threat in Northern India

Rahul Shil^{1*}¹Associate Professor & Ph.D. Researcher, Department of MSN (Neuroscience), Victory College of Nursing, Harsha Institutions, Bengaluru-562123, IndiaDOI: [10.36348/sjmps.2023.v09i10.002](https://doi.org/10.36348/sjmps.2023.v09i10.002)

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*Corresponding author: Rahul Shil

Associate Professor & Ph.D. Researcher, Department of MSN (Neuroscience), Victory College of Nursing, Harsha Institutions, Bengaluru-562123, India

Abstract

Scrub typhus is not a recent disease. This was prominent before the era of World War II. However, the disease is primarily prevalent in the Pacific Islands and southeast Asia. The symptoms begin with fever, eschar development, and a rash. As a result, diagnosing the disease has become more complex because comparable symptoms can be observed in a variety of other conditions. Therefore, proper diagnostic tests are required to diagnose the condition. Scrub typhus infections are increasing in India every year, and several states are reporting an increase in cases. The disease mostly affects the gastrointestinal system, nervous system, renal systems, and respiratory systems; however, mortality can be minimized with early diagnosis and adequate treatment. As many people in India are unaware of the condition, raising awareness will help in the saving of many lives.

Keywords: Scrub Typhus, Public health, Northern India.**Copyright © 2023 The Author(s):** This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Scrub typhus, commonly known as bush typhus, is a bacterial infection caused by *Orientia tsutsugamushi*. Scrub typhus is transmitted to humans through the bites of infected chiggers (larval mites), which create infections in humans [1]. Trombiculid mite larvae (chiggers) feed on forest and rural rodents such as rats, voles, and field mice, which transmit *O. tsutsugamushi*. Mites serve as both a vector and a natural reservoir for *O. tsutsugamushi*. Scrub typhus, on the other hand, is also linked to rickettsial illnesses. Scrub typhus is generally prevalent in the Asia-Pacific region, surrounded by Japan, Korea, China, India, and northern Australia [2].

The disease was discovered in northern Australia, Japan, and Southeast Asia in 1899, and it was then thoroughly researched from 1906 to 1932 [3]. This disease is also known as the 'tsutsugamushi triangle', since it is most prevalent throughout Southeast Asia. "Scrub typhus is likely one of the region's most underdiagnosed and underreported febrile infections that require hospitalization," the WHO stated in the year 1999. This opinion is still valid today, and scrub typhus is likely the world's most widespread, under-recognized, ignored, and severe but easily curable disease. Scrub

typhus first appeared in 2003–2004, when a few pediatric patients presented with fever, hepatosplenomegaly, and eschar. The National Center for Disease Control in New Delhi performed serological confirmation. In the sub-Himalayan region, outbreaks were also reported from Jammu to Nagaland, as well as in Himachal Pradesh, Pondicherry, Tamil Nadu, Sikkim, and Darjeeling. Outbreaks are more common during the rainy season; however, in South Indian states, outbreaks have been confirmed in the winter months as well [4]. According to the latest news, there has been a surge in the cases in Odisha, Rajasthan, and Kerala, where the number has increased to 193, with 10 (in 2023) fresh new cases in Odisha and [5] and 854 cases (in 2023) in 35 days in Rajasthan [6]. Humans are unintentional hosts for this zoonotic disease, and people of all ages, including children, are also affected. While scrub typhus is geographically restricted to Asia Pacific, a billion people are in danger, with over a million cases reported each year where the fatality rates range from <1% to 50%, depending on the antibiotic treatment, the individual affected, and the strain of *O. tsutsugamushi* found [7].

Recently, the number of scrub typhus cases has increased in India, mostly in the northern part of India. Even though the mortality rate is lower, there are no vaccines available to treat the disease. Therefore, there is

a serious public health concern growing in India related to the disease.

Transmission

Some species of infected trombiculid mites, such as *Leptotrombidium deliense* and chiggers, which feed on tissue fluid and lymph rather than blood, spread the infection to people and rodents. By consuming the bodily fluid of tiny mammals, such as rodents, they become infected and continue to carry it throughout their life cycles. As adults, they transmit the disease to their eggs through a mechanism known as transovarial transmission. As the mites are so small (0.2–0.4 mm), it requires a magnifying glass or microscope to see them. The infection spreads by a process known as transtadial transmission from the egg to the larva or adult, where Chigger mite populations are able to sustain their

infectivity on their own for a prolonged period of time. Mite larvae prefer to put their mouthparts down on hair follicles or pores rather than biting or piercing the skin. The salivary glands of the larvae contain a significant amount of *Orientia tsutsugamushi*, which is injected into its host as it eats. Following that, the black eschar mark will be left behind.

Life Cycle

A person becomes infected when he unintentionally touches an infectious larval mite while standing, sitting, or lying on infested ground. The lifecycle of adult mites consists of four stages: egg, larva, nymph, and adult. Since the other life stages (nymph and adult) do not feed on vertebrate animals, only the larval stage of the chigger may spread the disease to people and other vertebrate animals [8].

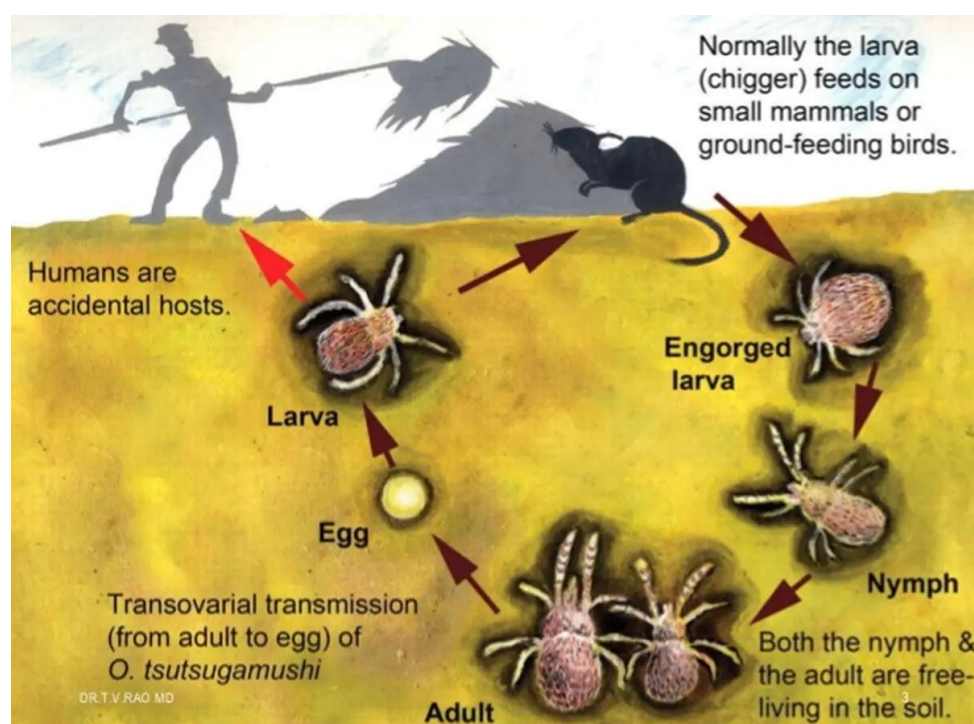


Fig-1: Transmission of scrub typhus

Clinical Features:

Generally, 1 to 2 weeks after being bitten, the symptoms appear, such as fever, chills, sweating, headache, cough, swollen glands, and occasionally a dull red rash. The bite site frequently develops an "eschar," or core black scab, along with ulcers and redness. 55% of patients in a recent South Indian study had an eschar, which was [9] found to be more common in South Asian patients than in East Asians or Caucasians. The clinical traits of eschar formation, however, showed an inconsequential distribution. Males' primary sites of presence were the axilla, groin, and genitalia (55.8%), whereas females' primary sites of presence were the chest and belly (42.3%). Eschar was reportedly found in unusual places, including the dorsum of the foot, earlobes, and cheeks.

Scrub typhus infection has been associated with a number of neurological symptoms, such as meningitis, meningoencephalitis, and encephalitis, which are the three neurological symptoms of scrub typhus that occur most frequently. Other conditions include facial palsy, abducens nerve palsy, bilateral optic neuritis, cerebellitis, Guillain-Barre syndrome, transient Parkinsonism, myoclonus, opsoclonus, transverse myelitis, polyneuropathy, and transverse myelitis [10]. Also, an unusual presentation can happen, which can be accompanied by an acute abdomen, particularly in patients from hyperendemic regions. Additionally, severe scrub typhus infections have also been linked to multi-organ failure and hemorrhage, both of which are deadly without treatment [1].



Fig-2: Eschar formation on skin



Fig-3: Eschar formation later stage

Diagnosis:

There are a number of symptoms of scrub typhus that are similar to many other diseases, so it becomes crucial for the healthcare fraternity to recognize the differences between the symptoms. Eschar development in the skin and a constant high temperature are the predominant complaints; thus, investigations should be done to identify the illness. One of the most essential elements for the diagnosis of scrub typhus are serological tests. The micro-immune-flouescence test is also considered the best preferred. However, some of the other tests available are immunoperoxidase assay, ELISA, polymerase chain reaction (PCR), latex agglutination, indirect haemagglutination, etc [11]. The *Proteus mirabilis* OXK carbohydrate antigen is used to identify scrub typhus. The most commonly used test now is the Weil-Felix OX-K agglutination reaction (WF test). Also, it is inexpensive, easy to perform, and results are quick. The WF test depends on identifying agglutinin in different *Proteus* strains that respond to agglutigen from *Rickettsia* species when they cross-react. IgM-type titers are detected in the primary infection mostly at the end of the first week. Furthermore, IgG titers are detected at the end of the second week. The *Proteus mirabilis*

OXK carbohydrate antigen is used to identify scrub typhus. Recent data suggests that WF is the most commonly performed and extensively used serological test in underdeveloped countries. However, indirect immunofluorescence antibody (IFA) is also a gold standard for detection. IFA is a costly diagnostic procedure, but the results can be produced in a matter of hours. Therefore, this test can confirm the diagnosis before seroconversion. Moreover, immunochromatographic testing, also known as ICT, is a quick diagnostic procedure for measuring antibody levels [12]. The market has recently seen the arrival of commercial rapid detection kits like Dip-STICKS, Multies Dip-S-Ticks Scrub Recombinant Assay, scrub typhus IgM and IgG Rapid Immunochromatographic Assay, and scrub typhus RCT, but due to their expensive cost, most developing countries still cannot afford them [13].

Proper samples are important for the diagnosis. Therefore, Eschar samples can be utilized for PCR tests. Lymph node biopsies, ethylenediaminetetraacetic acid blood, and skin rash samples can also be used for polymerase chain reaction (PCR)-based molecular detection. However, real-time PCR tests based on GroEL

are far more precise and provide more quantitative results. Bilateral pleural effusion is possible, which can be detected by chest X-rays. Also, an ultrasonography test may show enlargement of the liver and spleen. Creatinine elevation is also possible in some of the more severe cases [7].

Treatment

Currently, there are no gold standard treatments available as there are no vaccines available to prevent scrub typhus. However, antibiotics are found to be effective in elevating symptoms and reducing mortality rates. The preferred medication for treating scrub typhus is doxycycline, although tetracycline is also frequently used. Scrub typhus can be treated with doxycycline (2.2 mg/kg/dose twice PO or IV, maximum 200 mg/day for 7–15 days) and tetracycline (25–50 mg/kg/day split every 6 hours PO, maximum two g/day per mouth, for 7–15 days). A single dose of 200 mg of tetracycline may be taken for prophylaxis. One possibility for alternative regimens is chloramphenicol (500 mg QID orally for adults for 7–15 days; 50–100 mg/kg/day split every 6 hours intravenously; maximum 3 g/24 hours). The selection of efficient antibiotics is also difficult due to the discovery of excellent resistance [12]. Chloramphenicol should not be used during pregnancy, and the dose should be decreased in patients with liver impairment. It should also be continued for at least 5 days if the fever does not subside [7]. Patients who do not respond well to conventional treatment rifampicin, 900 mg per day for a week, have been found effective [11]. Azithromycin, rifampicin, and roxithromycin are some antibiotics that have been proven to be beneficial. However, in numerous studies, rifampicin has been found to be superior to doxycycline. Chemoprophylaxis with doxycycline (200 mg weekly) can stop the disease from becoming a bigger problem, but it additionally opens the door for infection. According to reports, roxithromycin (150 mg twice a day) is just as effective as doxycycline [7].

Prevention:

If there is a rise in scrub typhus cases, prevention is one of the most crucial aspects to consider. Prevention, prophylactic treatment, and curative treatment are the main three phases of the preventive aspect. The most important factor is recognizing the threat that chiggers may pose. Below are some points that can be taken into consideration.

- Traveling should be kept to a minimum in locations where scrub typhus is an ongoing threat, and people should stay away from densely forested and bushy areas where chiggers are widespread.
- The child should wear clothes that can cover their arms and legs.
- The travelers should use environmentally friendly insect repellents that are approved by the EPA and contain DEET or other chemicals that provide effective chigger protection.

- Clothing and equipment should be cleaned with 0.5% permethrin or equivalent solutions if they have been exposed to regions where chiggers are prevalent [1].

Recent research done on antibiotics for scrub typhus, which was published in the Cochrane review, has made the following observations:

- The comparative effectiveness of various broad-spectrum antibiotics in treating scrub typhus is not yet confirmed because of insufficient evidence.
- Tetracycline and doxycycline are comparable to one another and have been used to treat this condition, and both seemed to be effective in the few patients on whom the research was done.
- In locations where scrub typhus responds weakly to conventional anti-rickettsial medications, rifampicin is seen to be more effective than doxycycline.
- Clinicians should monitor the progress of patients in light of reports of drug resistance.
- The patient's progress should be monitored thoroughly in case of drug resistance.
- To assess the use of antibiotics in scrub typhus, additional research is needed. If diagnostic test results were readily available, it could have been easy to run the trial, and the results could have been easily interpreted. Such a result could pave the way to understanding whether or not a single dose of doxycycline is as effective as a three- or five-day course of treatment.
- It is important to assess the treatment plans for serious diseases, for example, by comparing intravenous chloramphenicol with intravenous tetracycline.
- Alternative antibiotics (azithromycin and ciprofloxacin) need to be studied further, especially in regions where scrub typhus appears to respond poorly to anti-rickettsial medications [13].

CONCLUSION

Scrub typhus can be deadly if treated too late. As a result, life-threatening complications can occur among patients, such as gastrointestinal hemorrhage, renal failure, encephalitis, pneumonia, and myocarditis [13]. Since vaccines are not available yet and the fresh trials have been found ineffective, Therefore, some of the available treatment choices are very expensive, and there are few diagnostic centers in developing countries, which is contributing to significant mortality. Early diagnosis and antimicrobial therapy have demonstrated significant benefits in preventing scrub typhus. However, further research is needed to determine the most effective therapeutic approach for preventing scrub typhus.

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