TYPE Opinion
PUBLISHED 14 May 2024
DOI 10.3389/fitd.2024.1371905

Check for updates

OPEN ACCESS

EDITED BY
Archana Shrestha,
Kathmandu University, Nepal

REVIEWED BY
Shih Keng Loong,
University of Malaya, Malaysia

*CORRESPONDENCE
Ranjit Sah
ranjitsah57@gmail.com
Ranjan K. Mohapatra
ranjank_mohapatra@yahoo.com

RECEIVED 17 January 2024
ACCEPTED 25 March 2024
PUBLISHED 14 May 2024

CITATION
Mohapatra RK, Al-Haideri M, Mishra S, Mahal A, Sarangi AK, Khatib MN, Gaidhane S, Zahiruddin QS, Mohanty A and Sah R (2024) Linking the increasing epidemiology of scrub typhus transmission in India and South Asia: are the varying environment and the reservoir animals the factors behind? *Front. Trop. Dis* 5:1371905. doi: 10.3389/fitd.2024.1371905



# Linking the increasing epidemiology of scrub typhus transmission in India and South Asia: are the varying environment and the reservoir animals the factors behind?

Ranjan K. Mohapatra [1*], Maysoon Al-Haideri [2], Snehasish Mishra [3], Ahmed Mahal [4], Ashish K. Sarangi [5], Mahalaqua Nazli Khatib [6], Shilpa Gaidhane [7], Quazi Syed Zahiruddin [8], Aroop Mohanty [9] and Ranjit Sah [10,11,12*]

[1]Department of Chemistry, Government College of Engineering, Keonjhar, Odisha, India, [2]Pharmacy Department, School of Medicine, University of Kurdistan Hewlêr, Kurdistan Region, Iraq, [3]School of Biotechnology, KIIT Deemed-to-be-University, Bhubaneswar, Odisha, India, [4]Department of Medical Biochemical Analysis, College of Health Technology, Cihan University-Erbil, Erbil, Iraq, [5]Department of Chemistry, School of Applied Sciences, Centurion University of Technology and Management, Bolangir, Odisha, India, [6]Division of Evidence Synthesis, Global Consortium of Public Health and Research, Datta Meghe Institute of Higher Education and Research, Wardha, India, [7]One Health Centre (COHERD), Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, India, [8]South Asia Infant Feeding Research Network (SAIFRN), School of Epidemiology and Public Health, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India, [9]Department of Clinical Microbiology, AIIMS Gorakhpur, Gorakhpur, Uttar Pradesh, India, [10]Department of Microbiology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India, [11]Department of Public Health Dentistry, Dr. D.Y. Patil Dental College, Hospital, Dr. D.Y. Patil Vidyapeeth, Pune, Maharashtra, India, [12]Department of Microbiology, SR Sanjeevani Hospital, Siraha, Nepal

KEYWORDS

**scrub typhus, epidemiology, transmission, India, Asia, diagnosis, One Health Approach**

## Introduction

Scrub typhus has become a focus of research after the thousands of confirmed cases and multiple deaths in 2023, in India in particular and in South Asia in general. Confirmed human cases of this zoonotic disease were reported throughout India, with 17 deaths. The Indian states of Himachal Pradesh (with nine deaths), Odisha (with eight deaths), and Rajasthan reported considerably high numbers during this period. Furthermore, Telangana State reported scrub typhus co-infections with dengue and flu. While the nine deaths in Himachal Pradesh were from the Shimla district, the eight confirmed deaths in Odisha were from two districts (https://www.hindustantimes.com/india-news/two-more-deaths-due-to-scrub-typhus-in-odisha-toll-rises-to-8-101694975575286.html). Kalahandi, Bargarh, Sundargarh, and Keonjhar were the four districts of Odisha where scrub typhus was dispersed, with Sundargarh and Keonjhar being the hardest hit. Sundargarh reported high dengue cases as well, adding further burden to the health department in the area. However, no co-infection was reported from this area at the time. The possible typhoid, dengue, or flu co-infections with scrub typhus would complicate the clinical symptoms in the affected cases, impacting the healthcare initiatives and overburdening the healthcare infrastructure (1), with the children, the immunocompromised, and the elderly at high risk.

The World Health Organization (WHO) has listed scrub typhus as an underacknowledged neglected disease of serious public health concern in the Asia Pacific region. In India, scrub typhus is of significant health concern (2–4). With considerably high reported cases in India—from the south (the states of Tamil Nadu, Karnataka, Andhra Pradesh, and Kerala), the north (the states of Uttaranchal, Himachal Pradesh, Jammu, and Kashmir), the northeast (the states of Assam, Meghalaya, and Nagaland), the east (the Odisha, West Bengal, and Bihar states), and the west (the states of Maharashtra and Rajasthan), in recent times, the disease has appeared to be prevalent in diverse ecological settings (3, 5). This is more so because India is as large as a continent (it is considered as a subcontinent nation) and the ecological conditions vary greatly across its length and breadth.

## The epidemiology

Grossly economically deprived countries, particularly in Africa and Asia, are already facing the burden of neglected tropical diseases as additional overdue health concerns (with Noma being added to the list by the WHO and the UN in December 2023) (6), of which scrub typhus is one. Scrub typhus is frequently reported as one of the most neglected tropical diseases from South Asia. The rural belts in Indonesia, China, Japan, and India (Southeast Asia), as well as northern Australia in the Indo-Pacific region, often report scrub typhus cases as a major cause of undifferentiated acute febrile illness in the "Tsutsugamushi Triangle." Tsutsugamushi combines two Japanese words: "tsutsuga" meaning sickness and "mushi" meaning insect. Its first documentation (as *Orientia tsutsugamushi*) dated back to 313 AD in China. Once considered as strictly endemic to the Tsutsugamushi Triangle (from southeastern Siberia in the north to northern Australia in the south and the Kamchatka Peninsula in the east to Pakistan in the west), scrub typhus has since spread beyond its seemingly natural boundary. Scrub typhus has also been recently reported in Africa, Chile, Peru, and the Arabian Peninsula, suggesting that the disease is widely spreading (7).

Thus, scrub typhus has been reported globally from regions outside the Tsutsugamushi Triangle over the past decade (3), becoming a cause of concern for health organizations. Globally, it affects a million annually and poses a threat to another billion (8). Scrub typhus, caused by *O. tsutsugamushi*, affects anyone, without gender, race, or age group bias (9). Japan reported and described the first scrub typhus case in 1899. A total of 5,441 scrub typhus cases were reported within the US Army during the Second World War in the rural or jungle areas around the Pacific, which led to 283 deaths and which incapacitated thousands.

The epidemiology of scrub typhus varies geographically and is dependent on the climatic conditions, the species diversity of the etiological agent, and the transmitting arthropod vectors. Scrub typhus cases are frequently reported in high numbers from rural India and Southeast Asia during the monsoon and post-monsoon seasons (from June to November). Scrub typhus infection occurs in Japan, South Korea, Taiwan, and northern China exclusively during the spring and early winter. It is commonly encountered in Thailand, Burma, and India from June to November. Nevertheless, the prevailing environmental temperature, humidity, sunshine, and atmospheric pressure are clearly important factors in the development of chigger, which is the critical life stage that transmits the infection, although the extent of the dependency (or association) remains a topic of further scientific investigation. Seasonality in the northern latitude, where the temperature drops extremely low during the winter, may not be conducive for the chiggers to attach to the human body for feeding and sustenance (10). The *tsutsugamushi* life cycle in this area is therefore debatable and could be non-existent. The ideal microenvironment for the infectious vector to thrive is specific, i.e., unmaintained lush green areas, riverbanks, and forest clearings. Often referred to as scrub typhus islands, these are high-risk restricted areas for human activities. Moreover, due to the ambiguity in human pathogenicity, the epidemiology of scrub typhus is not fully understood (11). Efforts to prevent and control scrub typhus will aid in a better understanding of the disease and its epidemiology.

A Malaysian study observed that there is a likely higher risk of chigger bites and scrub typhus infection during the dry season due to the abundant presence of the vector (12). Thick greenery bordering forest areas could be a suitable niche for a larger vector population. Reducing the population of small mammals and the relative humidity could be possible ground-level options to address and reduce the risk of scrub typhus (12). Nonetheless, anthropogenic activity is a key risk determinant. Spatial and seasonal understanding of the host and chigger networks near human habitats and the microdynamics of *O. tsutsugamushi* is needed.

## The agent and vector

In general, scrub typhus infection is seasonal, with an approximately 4- to 21-day incubation period. Although preventable, scrub typhus is fatal without a timely intervention, with complications including interstitial pneumonia, meningoencephalitis, and myocarditis (https://ncdc.mohfw.gov.in/WriteReadData/linkimages/ScrubTyphusBook.pdf). *O. tsutsugamushi* is an obligate intracellular Gram-negative coccobacillus *Rickettsia*. Being zoonotic in origin, *O. tsutsugamushi*, the bacterial causative agent of scrub typhus, is primarily parasitic to chiggers of trombiculid mites (*Leptotrombidium deliense*), which are the primary carriers (13). *Leptotrombidium akamushi* (also named as *Trombicula akamushi*) is a closely related cousin of *L. deliense*. It typically inhabits lush vegetation regions, and the mite is infected during its larval stage (chigger) by wild rodents and other such small animals. Scrub typhus spreads to humans through the bite of infected chigger during the monsoon season, frequently mimicking other monsoon illnesses such as dengue and malaria.

## The symptoms

An epidermal sore (eschar, a skin ulcer with a dark center) appears at the site of the bite of an infected chigger. Following this, symptoms such as fever, chills, headache, rash, lymphadenopathy, muscle pain, and body ache would develop. The clinical symptoms vary, ranging from acute undifferentiated febrile illness to multi-organ failure (3, 14). Children with scrub typhus are more prone than adults to hypoxia, hypoglycemia, and dyselectrolytemia (9). A prudent early diagnosis approach is used to observe whether the fever still continues beyond 5 days without dengue, malaria, or typhoid co-infection.

## The diagnosis

An early and meticulous diagnosis of scrub typhus could reduce complications and prevent mortality. The diagnosis of scrub typhus is challenging as it manifests similar symptoms, at least at the early stage, to other febrile illnesses such as dengue, influenza, and coronavirus disease 2019 (COVID-19). A misdiagnosis leading to delayed targeted medical interventions could be fatal, which further complicates the situation. Scrub typhus is serologically determined using the Weil–Felix test (WFT), enzyme-linked immunosorbent assay (ELISA), and molecular diagnosis through PCR of the isolated causative organism, *O. tsutsugamushi*. A study suggested that an ELISA involving immunoglobulin M (IgM) together with nested PCR (nPCR) provides a diagnostic advantage especially in endemic regions and could accurately diagnose and facilitate prompt treatment for scrub typhus (15).

Challenges in the diagnosis are also a concern in hilly regions with high rural tribal populations. Evaluation of the various associated factors, including the ecology on the transmission of scrub typhus in the area, such as the rodent population, the habitat characteristics, and the climatic conditions, is also essential (13). Community-based surveys and interdisciplinary research to accurately assess the disease burden and to effectively implement prevention strategies are imminent and emergent. The "One Health" model appears to be a technically sound, effective strategy; however, the necessary funding and the logistics involved in its timely implementation represent a challenge.

## The treatments

An early diagnosis followed by doxycycline or azithromycin (antibiotic) treatment is vital for a timely recovery. For adults, a bifurcated 7-day dosing of 200 mg/day doxycycline or a 5-day single dosing of 500 mg/day azithromycin is recommended. As doxycycline is contraindicated in those who are pregnant, the latter is recommended. In the case of severe illness or with cardiac, renal, pulmonary, or central nervous system complications, a patient is then referred to a well-equipped center (https://ncdc.mohfw.gov.in/WriteReadData/linkimages/ScrubTyphusBook.pdf). In children, a 4.5-mg/kg body weight bifurcated 7-day dosing of doxycycline or a 10-mg/kg body weight 5-day single dosing of azithromycin is recommended. As scrub typhus could potentially cause multi-organ failure and register higher mortality rates, a rapid diagnosis, the appropriate administration of antibiotics, and an enhanced surveillance are critical.

## Discussion

Typhus fever, a group of human-transmitted bacterial typhoid, is transmitted by chiggers, lice, fleas, and trombiculid mite chiggers in heavy scrub vegetation areas. The three typhoid forms are epidemic (spread by body lice), murine (spread by fleas), and scrub (spread by chiggers). Thick vegetation is the natural habitat of *L. deliense* (trombiculid mite), and thus the majority of scrub typhus cases occur in these areas. The most abundant scrub typhus vectors in Southeast Asia are *L. deliense* and *L. akamushi*, which are endemic to the geographical regions of Thailand, the Maldives, Indonesia, Nepal, Sri Lanka, Myanmar, and India (16). The chiggers of *Walchia disparunguis pingue*, *Walchia kritochaeta*, *Walchia oudemansi*, *Talinum paniculatum*, *L. deliense*, *Leptotrombidium arenicola*, *Eutrombicula wichmanni*, and *Ascoschoengastia indica* are reportedly active in human-modified environments such as dwelling areas, social forestry, and dumpsites, while those of *Walchia ewingi ewingi*, *Gahrliepia rutila*, and *Walchia rustica* are predominant in habitats bordering a forest (12). Another species, *L. arenicola*, has been reported to be found strictly in sandy beach ecology. However, *A. indica* is cosmopolitan (i.e., dwells in all habitat types), which is an extreme generalist and parasitizes all host types. According to recent reports, *W. kritochaeta* has an important role in scrub typhus epidemiological studies.

Due to the lack of rapid, reliable, and cost-effective diagnostic tools and infrastructure support, the timely diagnosis of scrub typhus is a challenge. The burden of this rickettsial infection, particularly in endemic belts, could be substantially high as the conventional WF test is not sensitive enough. However, a mixed infection as confirmed by the WF test could be verified using molecular techniques. Molecular assays can be adopted as alternative approaches as they are highly sensitive tools requiring relatively low infrastructure support, after verifying their feasibility in specific resource-limited settings. Another major reason for misdiagnosis or delayed diagnosis that leads to mortality is the lack of awareness about the disease (17). Although the major pathognomonic symptom is eschar, scrub typhus should still be suspected particularly in an endemic region even in the absence of an eschar (18).

The life cycle of trombiculid mites has four stages: the eggs, the larvae (or the chigger), the nymphs, and the adult. Of these, the nymphs and adults are capable of leading a free life on soil (19). Only chiggers transmit scrub typhus to vertebrates, including humans, as the other stages are not dependent on vertebrate blood to thrive. After being bitten by an infected mite, scrub typhus manifests in 7–10 days, which generally lasts 14–21 days without timely treatment. Scrub typhus is seasonal as the cases increase with "unmaintained" greeneries, especially during the monsoon. Although it mainly occurs among farming communities in close contact with vegetation, it also affects urban populations visiting the countryside or that are exposed to thick vegetation in parks. Farmers working in orchards and shrub areas and visitors to mite-infested isolated regions are both at high infection risk. Avoiding "mite islands" (the ecological niche where mites/chiggers thrive) is therefore advisable. Moreover, avoiding areas with heavy vegetation, which have a high possibility of mite sighting, is recommended to prevent contact with infected chiggers. Care must be taken while visiting shrubby fringes, grassy fields, poorly maintained gardens, riverbanks, sandy beaches, and abandoned greeneries. Furthermore, mites have been observed on animal bodies (such as mice and rats) as well.

When physical avoidance is difficult to maintain, preventive measures including wearing protective clothing when engaged in general agricultural activities or when visiting bushy or shrubby areas, applying insect repellents (such as diethyltoluamide) on the exposed skin, and avoiding dense unmaintained vegetation or sleeping on the ground can be adopted (19). Chemicals such as benzyl benzoate, which can be applied on clothing and bedding, can be used to kill mites. In addition, the greenery (vegetation) around a house could be treated with insecticides. Rodent control measures and regular cleaning of animal sheds are also suggested.

Although scrub typhus is a threat only during the monsoon, it needs effective management throughout, which includes remaining vigilant, following the preventive measures laid out, and applying timely therapeutic interventions. Climatic and weather parameters, such as temperature, humidity, and rainfall, are the major factors contributing to scrub typhus incidence. A study observed that a rise in the mean temperature by a single degree Celsius increased the scrub typhus cases by 3.8% (20). The cases increased by 8.5% (95% CI = 2.7%–14.5%) with a 10% rise in relative humidity and by 0.9% (95% CI = 0.6%–1.2%) with a 10-mm increase in rainfall, with a 4-month lag in both cases. Himachal Pradesh recorded more than 1,000 scrub typhus cases in 2023, which was twice the number recorded in the previous year. There was a record-breaking rainfall in 2023 in this hilly and greenery-dominated state, which could have contributed to the spike in scrub typhus cases. As chiggers thrive well at low temperatures and high humidity, heavy rainfall and high humidity could have provided a favorable condition for chiggers harboring *O. tsutsugamushi* to thrive. The usual time for the larvae of mites to surface after the monsoon is from July to October, and this is the period when most of India has high humidity and low temperature. In particular, the western parts of Odisha witnessed a climatic condition during the monsoon and thereafter in 2023 that might have been favorable for the mites to thrive.

The temperature regime during the monsoon is also ideal for chiggers harboring the propagation of *O. tsutsugamushi*. Thus, the potential for infection is high while engaging in agricultural activities just as the monsoon sets in (21). Rodent hosts including *Rattus flavipectus*, *Apodemus agrarius*, *Rattus rattoides*, and *Suncus murinus* are often the major carriers of *O. tsutsugamushi* (20). Therefore, the weather conditions and the rodent population (being the major carrier) both play critical roles in the transmission of scrub typhus and need due consideration in order to prevent and control this potentially fatal disease.

Reports that focused on investigations linking scrub typhus and environmental variables are scarce. Studies associating rodent populations with the transmission rates of scrub typhus in varying climatic conditions, i.e., temperature, rainfall, and relative humidity, are also limited. The quantitative relationship between varying climatic conditions and scrub typhus transmission, especially in endemic regions, remains to be clarified. Environmental variables are widely used as indicators for the transmission risk of several rodent-borne illnesses (22–24). Analyses of the environmental factors and the animal carriers using extensive models that explain their effects on scrub typhus incidence are suggested. Socioeconomic factors, such as the economic status, seamless and equal distribution of health resources, and the average associated knowledge on scrub typhus among the general public, need to be surveyed and investigated. Surveillance targeted on scrub typhus particularly in endemic regions in order to monitor the trends and the outcomes of the various measures adopted should be established.

Analysis of sample DNA sequences suggested that Karp-related strains are seriously infectious. Defined by four (I, II, III, and IV) domain variabilities in the 56-kDa protein (exhibiting large antigenic variations) (25), the Karp genotype is the most prevalently (about 50%) responsible for scrub typhus cases (26, 27). Molecular characterization revealed a close association with the Karp-like Linh.DT strains reported earlier from Vietnam (9). Genome analyses of *O. tsutsugamushi* combined with whole-genome sequencing of suspected samples from various regions could be performed to better understand the mechanism of infection and to develop a robust method/protocol for early detection (15).

*O. tsutsugamushi* is reportedly often isolated from forest rodents (*Rattus sabanus*) and squirrels (*Callosciurus notatus*) in South Asia (28). With anthropogenic activities including microscale deforestation (tree cutting) and road construction (for transportation) and natural phenomena such as eroding banks (due to the meandering of rivers and streams), the wild habitats within rainforests could be affected (29), thereby extending the environment suitable for rodents and chiggers to increase in number (30). Data on the association of scrub typhus with the density of rodents or squirrels are scarce (28, 31). *L. arenicola* has been reported to be associated with *O. tsutsugamushi* in the infection of small mammals. The critical challenges in understanding the ecology of scrub typhus and in addressing the associated health issues include the specific role of small mammals, the habitat type, and the underlying risks to human life.

As birds are migratory in nature, their possible critical role in the spread of the disease over a wider geographical area and in the creation of new hot spots could not be ruled out. A similar role of migratory birds in the spread of infectious disease-carrying ticks has been reported (32). Shorebirds were parasitized by *Schoengastia archaea* and *Neacariscus* sp. Wild birds in forests showed *Odontacarus audyi*, *Neoschoengastia* spp. (*Neoschoengastia longipes* and *Neoschoengastia solitus*), and *Toritrombicula* sp. Thai domestic chicken was reported to have *Neoschoengastia gallinarum*, *E. wichmanni*, *Helenicula comata*, and *O. audyi* as parasites (33). In Malaysia, Galliformes (such as domestic chicken) has been reported to be the sole host of the chiggers of *N. gallinarum*. Kingfisher (Coraciiformes: Alcedinidae) in Malaysian provinces harbored

*Parascoschoengastia heynemani* (33). Wild birds that harbored the chiggers tested positive for *O. tsutsugamushi* (28). The breeding sites of a few bird species are allegedly suitable and support the life cycle of chiggers. Migratory birds could disperse chiggers such as *S. archaea* and *Neacariscussulae*, which could lead to the chiggers being extensively disseminated over a large region. The Southeast Asian forest biotope is highly variable for chigger-disseminating avian fauna and should be investigated in detail. In such a scenario, the risks due to human activities and inadvertent exposure should be given due consideration. Chiggers would not attach to the human body without enough opportunities. Population movements across the porous borders of Southeast Asia in an unhindered and unaccounted manner for economic reasons could provide high opportunities for human–chigger interactions and further spread the disease. Cause–effect analyses showed that a major economic growth of an area directly influences the increased rodent population in the locality, corresponding with the booming population. This could possibly add to the increased risk of transmission of scrub typhus. Studies on the role of migratory birds would provide useful data on the infection and transmission dynamics and for the prediction of potential risk areas (28). In addition, the use of statistical techniques and modeling will further help fill the critical gaps in the understanding of the ecology and disease risk of scrub typhus.

Taking everything into account, a coordinated comprehensive strategy to deal with diseases involving carriers, vectors, and pathogenic microbes needs to be developed to ensure a far-reaching impact in the long term. As a technically sound and effective method, the various relevant departments and agencies, including the stakeholders at the grassroots level, could work together under the "One Health" umbrella (34). Although its implementation is time-consuming and fund-intensive and requires a logistically demanding proposal, it could ensure sustainable health and the well-being of all living forms with equitable and judicious resource use. To achieve this, human doctors (physicians or clinicians), paramedics (clinicians, pharmacologists, or pathologists), animal doctors (veterinarians), community health experts, experts on infectious diseases and epidemiology, ecologists, environmentalists, and similar other investigators and surveyors need to join hands and share their acquired knowledge, expertise, and resources in association with other grassroots stakeholders.

## Author contributions

RM: Writing – original draft. MA-H: Data curation, Writing – original draft. SM: Writing – original draft. AMa: Data curation, Writing – original draft. AS: Writing – review & editing. MK: Writing – review & editing. SG: Writing – review & editing. AMo: Writing – review & editing. QZ: Writing – original draft. RS: Writing – review & editing.


## Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.


## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

## Publisher's note



## References


1. Mohapatra RK, Mahal A, Mishra S, Kandi V, Obaidullah WJ. SARS-CoV-2 variants BA.2.86 and EG.5.1 alongside scrub typhus and Nipah in India during the ongoing cricket world cup 2023: threat perceptions and countermeasures. *Cureus*. (2023) 15:e48895. doi: 10.7759/cureus.48895

2. WHO. *World Health Organization Department of Communicable Disease Surveillance and Response. WHO Recommended Surveillance Standards* (19991999). Geneva: World Health Organization. Available at: https://apps.who.int/iris/handle/10665/65517 (Accessed 5 January 2024).

3. 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. doi: 10.1371/journal.pntd.0006062

4. Saraswati K, Day NP, Mukaka M, Blacksell SD. Scrub typhus point-of-care testing: a systematic review and meta-analysis. *PLoS Negl Trop Dis*. (2018) 12:e0006330. doi: 10.1371/journal.pntd.0006330

5. Devasagayam E, Dayanand D, Kundu D, Kamath MS, Kirubakaran R, Varghese GM. The burden of scrub typhus in India: A systematic review. *PLoS Negl Trop Dis*. (2021) 15:e0009619. doi: 10.1371/journal.pntd.0009619

6. Mohapatra RK, Mishra S, Kandi V, Rustagi S, Gaidhane AM, Satapathy P, et al. WHO officially recognises Noma as a NTD: Suggested global scale countermeasures. *Int J Surg Open*. (2024) 62(2):171–3. doi: 10.1097/IO9.0000000000000027

7. Walker DH. Scrub typhus—Scientific neglect, ever-widening impact. *N Engl J Med*. (2016) 375:913–5. doi: 10.1056/NEJMp1608499

8. Zaman K. Scrub typhus, a salient threat: Needs attention. *PLoS Negl Trop Dis*. (2023) 17:e0011427. doi: 10.1371/journal.pntd.0011427

9. Kaur J, Sharma N, Kanaujia R, Bisht K, Goel S, Biswal M, et al. Molecular characterization of Orientia tsutsugamushi causing fatal scrub typhus in a young male affected by so-called "mystery fever" in North India. *Indian J Med Microbiol*. (2023) 46:100418. doi: 10.1016/j.ijmmb.2023.100418

10. Moniuszko H, Makol J. Host-parasite association in trombiculid mites (Actinotrichida: Trombiculidae) of temperate zone—the case of Hirsutiella zachvatkini (Schluger 1948); are we dealing with prolonged contact with the host? *Parasit Vectors*. (2016) 9:61. doi: 10.1186/s13071-016-1339-2

11. Walker DH, Fishbein DB. Epidemiology of rickettsial diseases. *Eur J Epidemiol*. (1991) 7:237–45. doi: 10.1007/BF00145672

12. Alkathiry H, Al-Rofaai A, Ya'cob Z, Cutmore TS, Mohd-Azami SNI, Husin NA, et al. Habitat and season drive chigger mite diversity and abundance on small mammals in peninsular Malaysia. *Pathogens*. (2022) 11:1087. doi: 10.3390/pathogens11101087

13. Konyak BM, Soni M, Saikia S, Chang T, Gogoi I, Khongstid I, et al. Scrub typhus in Northeast India: epidemiology, clinical presentations, and diagnostic approaches. *Transact Royal Soc Trop Med Hygiene*. (2023) 118(3):206–22. doi: 10.1093/trstmh/trad082

14. Alam AM, Gillespie CS, Goodall J, Damodar T, Turtle L, Vasanthapuram R, et al. Neurological manifestations of scrub typhus infection: A systematic review and metaanalysis of clinical features and case fatality. *PLoS Negl Trop Dis*. (2022) 16: e0010952. doi: 10.1371/journal.pntd.0010952

15. Seetha D, Nori SRC, Nair RR. Molecular-based study of scrub typhus in Kerala, South India from 2014 to 2021: a laboratory-based study. *Comp Clin Pathol*. (2023) 32:347–56. doi: 10.1007/s00580-023-03443-8

16. Chakraborty S, Sarma N. Scrub typhus: An emerging threat. *Indian J Dermatol*. (2017) 62:478–85. doi: 10.4103/ijd.IJD_388_17

17. Malone SL, Staudhammer CL, Oberbauer SF, Olivas P, Ryan MG, Schedlbauer JL, et al. El Niño southern oscillation (ENSO) enhances CO2 exchange rates in freshwater marsh ecosystems in the Florida everglades. *PLoS One*. (2014) 9:e115058. doi: 10.1371/journal.Pone.0115058

18. Tarai B, Sen P, Kanaujia R, Kaur J, Biswal M, Das P. Epidemiological, clinical and genetic characterization of scrub typhus in patients presenting with acute febrile illness in New Delhi. *Indian J Med Microbiol*. (2022) 40(4):552–6. doi: 10.1016/J.IJMMB.2022.07.008

19. Mohapatra RK, Mishra S, Tuglo LS, Kandi V, Mohanty A, Sah R. Health emergency with recent surge of scrub typhus alongside other infectious diseases in India with Odisha in focus: Suggested mitigation measures and preparedness of public healthcare infrastructure. *New Microbes New Infections*. (2024) 56:101216. doi: 10.1016/j.nmni.2023.101216

20. Wei Y, Huang Y, Li X, Ma Y, Tao X, Wu X, et al. Climate variability, animal reservoir and transmission of scrub typhus in Southern China. *PLoS Negl Trop Dis*. (2017) 11:e0005447. doi: 10.1371/journal.pntd.0005447

21. Vanramliana, Pautu L, Lalmalsawma P, Rosangkima G, Sarma DK, Chinzah H, et al. Epidemiology of scrub typhus and other rickettsial infections, (2018–22) in the hyper-endemic setting of Mizoram, North-East India. *PLoS Negl Trop Dis*. (2023) 17: e0011688. doi: 10.1371/journal.pntd.0011688

22. Ostfeld RS, Canham CD, Oggenfuss K, Winchcombe RJ, Keesing F. Climate, deer, rodents, and acorns as determinants of variation in lyme-disease risk. *PLoS Biol*. (2006) 4:e145. doi: 10.1371/journal.pbio.0040145

23. Yan L, Fang LQ, Huang HG, Zhang LQ, Feng D, Zhao WJ, et al. Landscape elements and Hantaan virus-related hemorrhagic fever with renal syndrome, People's Republic of China. *Emerg Infect Dis*. (2007) 13:1301. doi: 10.3201/eid1309.061481

24. Zhang W, Guo W, Fang L, Li C, Bi P, Glass GE, et al. Climate variability and hemorrhagic fever with renal syndrome transmission in northeastern China. *Environ Health Persp*. (2010) 118:915. doi: 10.1289/ehp.0901504

25. Ohashi N, Nashimoto H, Ikeda H, Tamura A. Diversity of immunodominant 56-kDa type-specific antigen (TSA) of Rickettsia tsutsugamushi. Sequence and comparative analyses of the genes encoding TSA homologues from four antigenic variants. *J Biol Chem*. (1992) 267:12728–35. doi: 10.1016/S0021-9258(18)42337-X

26. Kelly DJ, Fuerst PA, Ching WM, Richards AL. Scrub typhus: the geographic distribution of phenotypic and genotypic variants of. *Clin Infect Dis*. (2009) 48:S203–30. doi: 10.1086/596576

27. Nguyen HLK, Pham HTT, Nguyen TV, Hoang PV, Le MTQ, Takemura T, et al. The genotypes of Orientia tsutsugamushi, identified in scrub typhus patients in northern Vietnam. *Trans R Soc Trop Med Hyg*. (2017) 111:137–9. doi: 10.1093/trstmh/trx022

28. Elliott I, Pearson I, Dahal P, Thomas NV, Roberts T, Newton PN. Scrub typhus ecology: a systematic review of Orientia in vectors and hosts. *Parasites Vectors*. (2019) 12:513. doi: 10.1186/s13071-019-3751-x

29. Traub R, Wisseman CL Jr. Current concepts of the ecology of chiggerborne rickettsiosis (scrub typhus). *Jpn J Med Sci Biol*. (1974) 27:1–5. doi: 10.7883/yoken1952.27.1

30. Audy JR. A summary topographical account of scrub typhus 1908–1946. Studies in the distribution and topography of scrub typhus, Number 1. *Bull Inst Med Res Malaya*. (1949) 1:1–82.

31. Mohd-Azami SNI, Loong SK, Khoo JJ, Husin NA, Lim FS, Mahfodz NH, et al. Molecular surveillance for vector-borne bacteria in rodents and tree shrews of peninsular Malaysia oil palm plantations. *Trop Med Infect Dis*. (2023) 8:74. doi: 10.3390/tropicalmed8020074

32. Scott JD. Studies abound on how far north Ixodes scapularis ticks are transported by birds. *Ticks Tick Borne Dis*. (2016) 7:327–8. doi: 10.1016/j.ttbdis.2015.12.001

33. Koosakulnirand S, Rajasegaran P, Alkathiry HA, Chaisiri K, Round PD, Eiamampaih K, et al. On the taxonomy of chigger mites (Acariformes: Trombiculidae) parasitizing birds in Thailand and Malaysia, with the description of a new species. *Acarologia*. (2023) 63:1109–38. doi: 10.24349/yt89-g1ei

34. Murhekar MV, Vivian Thangaraj JW, Sadanandane C, Mittal M, Gupta N, Rose W, et al. Investigations of seasonal outbreaks of acute encephalitis syndrome due to Orientia tsutsugamushi in Gorakhpur region, India: A One Health case study. *Indian J Med Res*. (2021) 153:375–81. doi: 10.4103/ijmr.IJMR_625_21