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RESEARCH ARTICLE

Scrub Typhus: Indian Situation and Current Report Generated by Indian Council of Medical Research-National Centre for Disease Informatics and Research under the Right to Information Act, 2005-reg

Shivam Rathor

Department of Bachelor of Pharmacy, Mandsaur Institute of Pharmacy, Mandsaur University, Mandsaur, Madhya Pradesh, India

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ABSTRACT

Scrub typhus infection in humans is caused by the obligatory, intracellular bacteria *Orientia tsutsugamushi*. This study explains the introductive part, historical background, epidemiology, pathogenesis, diagnosis, Indian situation of scrub typhus and the methodology of the Indian Council of Medical Research-National Centre for Disease Informatics and Research (ICMR-NCDIR). The results of this study show that there were 32355 incidents of scrub typhus overall in 2022 and 54162 cases overall in 2023. According to the report from ICMR-NCDIR under the Right to Information Act, 2005-reg, a total of 36 states in India were examined in the years 2022 and 2023; of those, 4 states did not report any cases of scrub typhus, and 32 states reported confirmed cases of the 32 states, 4 did not report any reports about scrub typhus in 2022, and in 2023, all 32 states reported confirmed cases of the disease.

Keywords: ICMR-NCDIR report, Indian situation of scrub typhus, scrub typhus

INTRODUCTION

Scrub typhus infection in humans is caused by the obligatory, intracellular bacteria *Orientia tsutsugamushi*.[1] The World Health Organization has named scrub typhus one of the most underdiagnosed/underreported diseases in the world that frequently requires hospitalization. This underscores the need to a greater awareness of the carriers, outbreaks, and pathogenesis associated with this organism.[2,3]

The life cycle of a mite belonging to the Trombiculidae family (*Acari*: *Trombidiformes*) has four phases: protonymph, deutonymph, tritonymph, and adult. In addition, there is an egg and two six-legged stages, called pre-larva and larva.[4]

Although it is widely acknowledged which adults are the stage that overwinters, a number of these dormant instars may also offer the biological possibility of persisting during harsh climatic conditions, which might include overwintering. The sole stage of parasitism is larval mites, commonly referred to as chiggers. Mite larvae consume this dissolving tissue.[5] Each significant category of terrestrial vertebrates is attacked by larval trombiculid mites; however, the primary food source for mites in the taxa known to transmit *O. tsutsugamushi* is small mammals. Additional research has shown that the mites' non-specific manner of feeding on mammals is similar. It is evident that larval mites have limited host specificity and feed opportunistically on a wide range of animals.[6] There is a lot of antigenic diversity in the causative bacterium [Figure 1]. This sometimes fatal infection poses a threat to one billion people worldwide, spanning more than eight million kilometer across Pakistan in the west to Australia in the southeast and Japan in the direction of the east.[7]

***Corresponding Author:**
Shivam Rathor,
E-mail: mind.s.528@gmail.com

Figure 1: *Orientia tsutsugamushi*[8]

Humans contract it by the bite of a trombiculid mite larva. Subsequently, it results in severe vascular leakage that damages end organs, widespread vasculitis, and perivascular inflammation. Persons of any age and visitors from all over the world who have been to endemic places are susceptible to contracting the disease.[9]

Clinical characteristics, which include a high body temperature, migraine, myalgia, and gastrointestinal symptoms, often appear after an incubation period of 6–21 days. Scrub typhus is distinguished by an eschar that often starts as an initial papular lesion and later crusts to create a black ulceration with core necrosis, although its occurrence varies depending on the location. Clinical suspicion should serve as the foundation for the decision to start treatment, which should then be verified by serological testing.[10]

HISTORICAL BACKGROUND AND PHYSICAL[10-12]

By biting a virtually small, frequently colored larva of a trombiculid mite (chigger), *O. tsutsugamushi* is transmitted to humans (red). River or flooding fever is another name for the illness because infected chiggers occur more frequently in heavily vegetated areas during the wet season.

Although other locations may have rodents and mites, the term "scrub" was chosen because of the overall vegetation that fosters the chigger-host relationship. Only a few locations worldwide are home to the illness. It primarily results in eschar at the site of bite, which grows into a cigarette bundle and a black crust-like substance.

Scrub typhus death rates are still unknown; however, they range from 40% to 45% for patients that are not treated with antibiotics. However, given the severity of the condition is thought to vary based on geographic strains, infectious dose, patient age, and comorbidities, figuring out the real mortality can be difficult. Scrub typhus typically presents with organ-specific consequences.

The virus gradually swept across the majority of India. A native illness in various parts of Asia, particularly the east and west, is scrub typhus. Scrub typhus is becoming a major cause of severe fever disease with a greater death and fatality rate. It has expanded throughout India in recent years. Figure 2 illustrates the clinical manifestations and sign among hospitalized scrub typhus patients in India.

Headaches and fever are the most prevalent signs; however, there might also be vague symptoms. In addition to myalgia and stomach pain, infected patients may also have nausea, vomiting, and widespread lymphadenopathy. Clinical manifestations and indicators among Indian hospitalized scrub typhus patients. Scrub typhus A common nervous system symptom of scrub typhus is meningitis, which is described as an occurrence of headaches or nuchal stiffness accompanied by either altered senses or focal neurological abnormalities on history or examination. The more severe kind of meningoencephalitis, which affects a subset of patients, is marked by altered sensorium and seizures. It has been linked to multiorgan dysfunction syndrome and has a higher case-fatality rate if treatment is delayed.

EPIDEMIOLOGY[14]

Many Asian nations, including those in South and Southeast Asia, China, Korea, Japan, Taiwan, and other countries are home to the endemic scrub typhus the so-called Tsutsugamushi triangle [Figure 3]. Since the habitat of mites, or shrub vegetation, grows during the monsoon and immediately post-monsoon period (July-October), this is when the

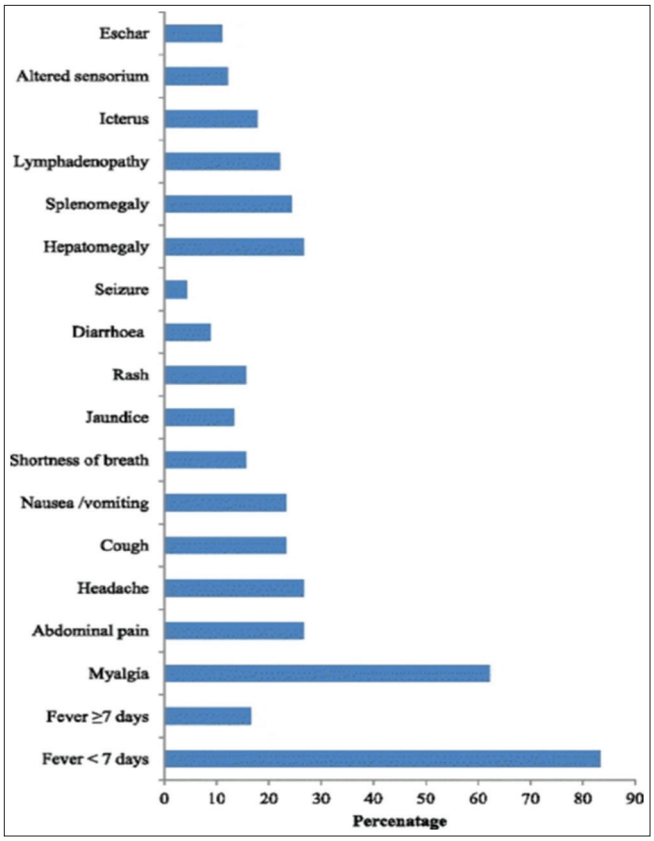

Figure 2: Clinical manifestations and sign among hospitalized scrub typhus patients in India[13]

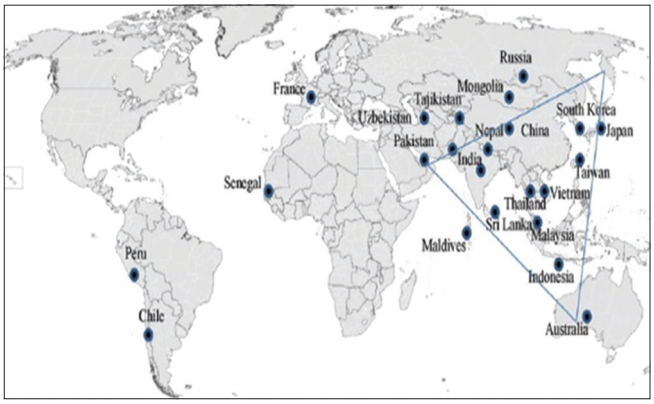

Figure 3: Map of the world with the Tsutsugamushi triangle[15]

infection primarily occurs. Less eschars, greater organomegaly, and a higher incidence of sequelae such as acute respiratory distress syndrome and macrophages activation syndrome are characteristics of the North Indian phenotype. On the other hand, coronary artery disease and acute kidney injury damage are more common in the South Indian phenotype. There are more cases of eschar in the Northeast, but there are also fewer complications and less organomegaly.

Scrub typhus in babies has a poorly understood fundamental epidemiology, with little information available on incidence and prevalence. This could be because the clinical presentation resembles that of other fever-causing factors quite a bit. In addition, the lack of diagnostic resources leads to incorrect diagnoses and underestimates the severity of the illness. Based on the existing information on newborns and kids, the fundamentals of epidemiology are described.

Males of all ages are primarily affected by scrub typhus, while those who engage in outdoor activities are particularly susceptible. There are other risk factors that are linked to this, such as farming in endemic areas, living close to a village's edge, scrub vegetation, ditches, and wood piles. Since they spend most of their time indoors, infants are less affected – the precise prevalence is unknown. According to a study conducted in Odisha, India, it was 9.1% among babies. Deforestation and close proximity to domestic and wild animals appear to be factors that contribute to the development of scrub typhus in babies. These factors additionally bring mites into people's homes. Overcrowding, poverty, and inadequate domestic hygiene may have a compounding effect.

PATHOGENESIS[16]

Through transovarian transfer, arthropods naturally preserve the rickettsial infection. Humans can contract *O. tsutsugamushi* by the bite of a chigger larva that has regurgitated contaminated saliva during feeding. The chigger bite causes a papule, which develops into a vesicle, bulla, and then quickly sloughs off, leaving behind an eschar that looks like a cigarette burn and a shallow ulcer. The eschar is where *O. tsutsugamushi* multiplies and enters the bloodstream, causing fever, headache, myalgia, and non-specific prodrome.

Even though chiggers bite the extremities, they typically settle in the groin and axilla because these are warmer, more concealed areas of the body. The organisms infiltrate the reticuloendothelial cells and vascular endothelium, resulting in endothelial damage and a vasculitic process that is thought to be the underlying pathogenesis. Microvascular leakage and the development of microthrombi in

the heart, lungs, and central nervous system are caused by vasculitis. The majority of the clinical characteristics and consequences of scrub typhus are explained by this, in addition to the cytokine storm and elevated concentrations of interferon alpha, interleukin (IL)-8, and IL-15.

The disease is typically transmitted to people by an infectious arthropod vector's bite or excrement. The four life stages of the mite are the egg, nymph, larva, and adult. Human infection is only possible with the second type. Bacteria infiltrate vascular endothelial cells, resulting in microvascular ulcerations and diffuse vasculitis. These conditions trigger the activation of T, macrophage, and cytokine responses, which in turn cause significant vascular bleeding and end-organ damage in organs such as the kidneys, heart, and lungs. Numerous inflammatory processes are brought on by activated cells, and both endothelium and non-endothelial cells produce cytokines that can cause tissue death in the sick person as well as be beneficial (e.g., antibacterial). Serious issues such infectious liver disorders, renal failure, meningitis, encephalitis, and respiratory distress can be brought on by this kind of immune reaction.

DIAGNOSIS[17,18]

Early detection of an acute scrub typhus infection is critical for proper patient management because it guides the choice of the best course of treatment and prevents problems before they arise. Rapid, sensitive, and reasonably priced diagnostic techniques are typically unavailable in scrub typhus-endemic areas, forcing doctors to start empirical treatment based only on suspicion. This frequently results in incorrect diagnoses and poor patient care.

The primary way for diagnosing scrub typhus is by serological techniques. When an initial scrub typhus infection occurs, a notable immunoglobulin (Ig)M antibody titer develops at the finish of the first week, whereas significant levels of IgG antibodies often take two weeks to manifest.

Indirect Immunoperoxidase (IIP)

After changing the indirect immunofluorescent antibody (IFA) procedures, this test was implemented to address the aforementioned flaw. Results with IIP techniques are comparable to those obtained using IFA. But like with IFA, the different strains affect this test's sensitivity. Technical know-how is still required even though a fluorescence microscope is not used.

Enzyme-linked Immunosorbent Assays (ELISA)

Weil–Felix testing is currently preferred to obtain a serological detection in patients with acute scrub typhus infection because it possesses a limited sensitivity and resources for performing IFA are not regularly available in common laboratories. It combines a recombinant p56-kDa type-specific antigen of an *O. tsutsugamushi* strain with IgM antibodies produced toward each strain of Karp, Kato, Gilliam, and TA716 to identify acute infections. An effective test to detect a recent *O. tsutsugamushi* infection is IgM ELISA.

Polymerase Chain Reaction (PCR) Techniques

They have a significant benefit in that they can identify the infection sooner since they can identify the illness before antibodies are detectable by serological tests. Antibiotics may have an impact on the organism's direct detection, which raises problems. PCR may identify extremely small amounts of copies with excellent sensitivity and specificity, but its expensive cost prohibits regular diagnosis in endemic areas.

The IFA

This examination is regarded as the most reliable method for scrub typhus diagnosis. This approach has a number of drawbacks since it necessitates repeat testing to show the distinction between a fourfold increase in antibody titers during the acute phase of serum samples and their following convalescent phase. As a result, it is a diagnosis made after the fact and has minimal bearing on how an acute infection is first treated. A single strong antibody titer cannot be regarded as diagnostic if previous research on baseline seroprevalence levels in the local population has not been done.

THE INDIAN SITUATION OF SCRUB TYPHUS

With a million cases a year, scrub typhus has resurfaced as among the most prevalent and potentially fatal rickettsial illnesses. In India, it is a public health issue that is mostly disregarded.

Acute undifferentiated fever (AUF) has become a prevalent ailment that commonly results in hospitalization of patients, especially during the rainy and post-monsoon seasons between June and September. Dengue is the most prevalent manifestation of AUF illness (AUFI) in India, with enteric fever, malaria, and scrub typhus following closely after. Nearly every region in India has a high prevalence of AUFI. Research was carried out in India to determine the clinical spectrum and etiological agents of severe undifferentiated febrile fever.

It is imperative to comprehend the distinctions between an AUFI and pyrexia of unknown origin that was originally defined as an illness with several episodes of fever over 38.3°C that did not result in an official diagnosis shortly after 1 week of medical observation. Following Griffin, more research uses different classifications without mentioning any clear local indications of feverish sickness or distinct indicators of inflammation.[19]

METHODOLOGY

A report or information of scrub typhus obtained by the Indian Council of Medical Research-National Centre for Disease Informatics and Research (ICMR-NCDIR) under the Right to Information Act, 2005-reg in the year of 2022 and 2023 of all states in India. The Ministry of Health, the Government of India, and other Central or state governments collaborate closely with the ICMR-NCDIR to provide baseline data on non-communicable diseases for monitoring and evaluating programs and activities using

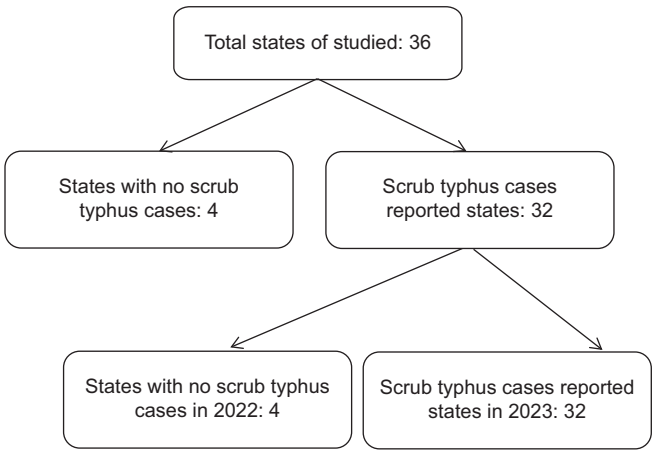

Figure 4: Scrub typhus reported rate

Table 1: States/UT-wise scrub typhus confirmed cases based on L form 2022 to 20233 from IHIP portal

S. No	States/UTs	2022	2023
1	Andaman and Nicobar Islands	0	0
2	Andhra Pradesh	597	980
3	Arunachal Pradesh	503	448
4	Assam	1023	1269
5	Bihar	45	86
6	Chandigarh	572	1052
7	Chhattisgarh	0	50
8	Delhi	100	274
9	Goa	0	0
10	Gujarat	0	8
11	Haryana	7	29
12	Himachal Pradesh	871	1832
13	Jammu and Kashmir	14	22
14	Jharkhand	0	20
15	Karnataka	729	1185
16	Kerala	14	793
17	Ladakh	0	0
18	Lakshadweep	0	7
19	Madhya Pradesh	142	914
20	Maharashtra	303	456
21	Manipur	216	204
22	Meghalaya	2873	6174
23	Mizoram	5771	12385
24	Nagaland	3904	5627
25	Odisha	984	3576
26	Puducherry	998	984
27	Punjab	69	103
28	Rajasthan	1524	2647
29	Sikkim	628	996
30	Tamil Nadu	5091	6161
31	Telangana	4	1
32	The Dadra and Nagar Haveli and Daman and Diu	0	0
33	Tripura	324	588
34	Uttarakhand	226	353
35	Uttar Pradesh	680	245
36	West Bengal	4143	4693
	Total	32355	54162

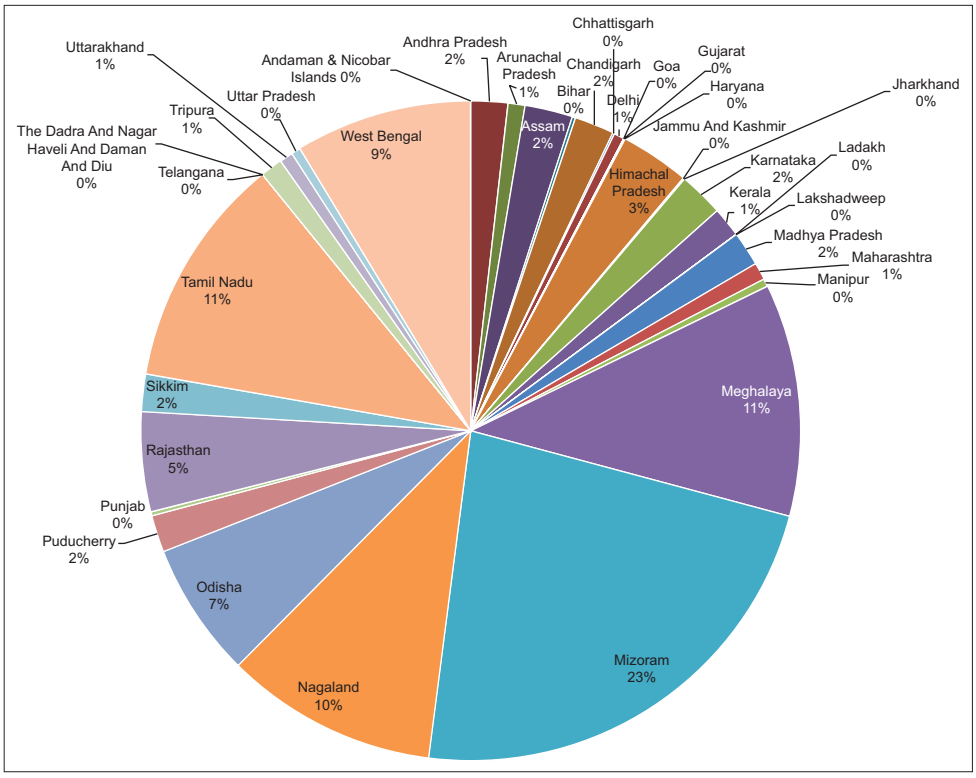

Figure 5: Pi chart representing scrub typhus cases in 2023

technology-based solutions. Retaining health data is the main benefit of supporting legal obligations in medicolegal cases. Furthermore, it permits data analytics and the evaluation of improved health outcomes in addition to making data recovery simple and the documentation process more efficient.

The field team entered the field using handheld devices that were loaded with the data collection software. The ability to save data backups on SD cards within the handheld was also available. The handheld devices' data were uploaded to and synchronized with the ICMR-NCDIR central server.

RESULTS

To determine the total number of cases of scrub typhus in all states of India, this systematic study will combine data collected from the ICMR-NCDIR under the Right to Information Act, 2005-reg in the year of 2022 and 2023 of all states in India [Figure 4].

Table 1 and Figure 5 illustrate that the total number of cases of scrub typhus in 2022 was 32355 and total number of cases of scrub typhus in 2023 was 54162. According to the report from ICMR-NCDIR under the Right to Information Act, 2005-reg in the year of 2022 and 2023 of all states in India, total 36 states were studied in which 4 states were not reported of scrub typhus cases and 32 states were reported confirm cases of scrub typhus. Among all 32 states, 4 states were not reported of scrub typhus cases in 2022 and all 32 states were reported confirm cases of scrub typhus in 2023.

According to this study, scrub typhus is highly prevalent in India and affects many organs in most individuals who test positive. Complications and fatality risk are raised by this. The public health concern associated with this disease can be mitigated in the future by raising knowledge of it, expanding access to testing, and starting the right treatment program early.

CONCLUSION

Scrub typhus grows more quickly throughout the nation as a result of resistance built up against various strains. The majority of infectious outbreaks

occur in Darjeeling, Meghalaya, and a few regions of Tamil Nadu. During the monsoon season, patients who appear with fever demand a higher level of suspicion. This study highlights that the total number of cases of scrub typhus in 2022 was 32355 and total number of cases of scrub typhus in 2023 was 54162.

REFERENCES

1. World Health Organization. WHO Recommended Surveillance Standards. Geneva, Switzerland: World Health Organization; 1999.
2. Izzard L, Fuller A, Blacksell SD, Paris DH, Richards AL, Aukkanit N, *et al*. Isolation of a novel *Orientia* species (*O. chuto* sp. nov.) from a patient infected in Dubai. J Clin Microbiol 2010;48:4404-9.
3. Balcells ME, Rabagliati R, Garcia P, Poggi H, Oddo D, Concha M, *et al*. Endemic scrub typhus-like illness, Chile. Emerg Infect Dis 2011;17:1659-63.
4. Huebner RJ, Jellison WL, Armstrong C. Rickettsialpox: A newly recognized rickettsial disease; recovery of *Rickettsia akari* from a house mouse (*Mus musculus*). Public Health Rep 1947;62:777-80.
5. Milhano N, Palma M, Marcili A, Núncio MS, de Carvalho IL, de Sousa R. *Rickettsia lusitaniae* sp. nov. isolated from the soft tick *Ornithodoros erraticus* (Acarina: *Argasidae*). Comp Immunol Microbiol Infect Dis 2014;37:189-93.
6. Lipovsky LJ. Studies of the food habits of postlarval stages of chiggers (Acarina, Trombicullidae). Univ Kansas Sci Bull 1954;36:943-58.
7. Mullen GR, Durden LA. Medical and Veterinary Entomology. Cambridge, CA, USA: Academic Press; 2009.
8. Available from: https://images.news18.com/ibnkhabar/uploads/2022/07/scrub-typhos-16579442303x2.jpg
9. Bonell A, Lubell Y, Newton PN, Crump JA, Paris DH. Estimating the burden of scrub typhus: A systematic review. PLoS Negl Trop Dis 2017;11:e0005838.
10. 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.
11. Rapsang AG, Bhattacharyya P. Scrub typhus. Indian J Anaesth 2013;57:127-34.
12. Rajapakse S, Rodrigo C, Fernando D. Scrub typhus: Pathophysiology, clinical manifestations and prognosis. Asian Pac J Trop Med 2012;5:261-4.
13. Available from: https://www.researchgate.net/publication/308881256/figure/fig1/AS:413683911020545@1475641338410/clinical-symptoms-and-signs-among-hospitalized-patients-with-scrub-typhus-meghalaya.png
14. 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.
15. Available from: https://jabonline.in/jab_demo/ckfinder/images/JABB-10-5-76-g002.jpg
16. Jamil M, Lyngrah KG, Lyngdoh M, Hussain M. Clinical manifestations and complications of scrub typhus: A hospital based study from North Eastern India. J Assoc Physicians India 2014;62:19-23.
17. Blacksell SD, Lim C, Tanganuchitcharnchai A, Jintaworn S, Kantipong P, Richards AL, *et al*. Optimal cutoff and accuracy of an IgM enzyme-linked immunosorbent assay for diagnosis of acute scrub typhus in Northern Thailand: An alternative reference method to the IgM immunofluorescence assay. J Clin Microbiol 2016;54:1472-8.
18. Anitharaj V, Stephen S, Pradeep J, Park S, Kim SH, Kim YJ, *et al*. Serological diagnosis of acute scrub typhus in Southern India: Evaluation of InBios scrub typhus detect IgM Rapid test and comparison with other serological tests. J Clin Diagn Res 2016;10: DC07-10.
19. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year. Lancet 2003;361: 2226-34.