

Invited Review

## **Rickettsioses in Sri Lanka – A mini review**

Veranja Liyanapathirana

*Sri Lankan Journal of Infectious Diseases 2019 Vol.9 (1):1-12*

DOI: <http://dx.doi.org/10.4038/sljid.v9i1.8239>

### **Abstract**

Rickettsioses are a group of vector-borne diseases that have come to the limelight in Sri Lanka during the last two decades. Evidence for spotted fever group rickettsioses, scrub typhus and other related diseases have been reported from Sri Lanka in a geographically restricted manner. This review summarizes the work done locally, that are publicly accessible as of 24<sup>th</sup> November 2018 with keyword searches ‘rickettsioses and Sri Lanka’, and ‘typhus and Sri Lanka’, on PubMed and Google Scholar. There is a considerable body of literature on rickettsioses in Sri Lanka, particularly as a result of collaborations with international research groups. These indicate that rickettsioses are found throughout the country, in a geographically restricted manner.

*Keywords: Rickettsioses, Typhus, Sri Lanka*

### **Introduction**

Rickettsial infections or rickettsioses are a group of vector-borne diseases. Organisms responsible belong to two genera; namely *Rickettsia* and *Orientia*. Other genera such as *Coxiella*, *Ehrlichia* and *Anaplasma* which were also originally classified among Rickettsial organisms are now in different taxonomic groups.<sup>1</sup> Rickettsioses were initially classified according to serological cross reactivity. However, they are also classified into different groups according to the causative organisms, vectors involved, clinical features and geographical distribution.<sup>2,3,4</sup>

---

<sup>1</sup>*Department of Microbiology, Faculty of Medicine, University of Peradeniya, Sri Lanka*

*Address for correspondence: Dr Veranja Liyanapathirana, Department of Microbiology, Faculty of Medicine, University of Peradeniya Telephone: +94777060887 Email: [veranjacl@yahoo.com](mailto:veranjacl@yahoo.com), [veranjacl@pdn.ac.lk](mailto:veranjacl@pdn.ac.lk)*

 <https://orcid.org/0000-0002-4356-2172>

---

Received 28 January 2019 and accepted 14 March 2019



This an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### **Typhus group**

The typhus group consists of *Rickettsia prowazekii* which causes epidemic typhus and *Rickettsia typhi* (formerly known as *Rickettsia mooseri*) which causes endemic typhus. *Rickettsia prowazekii* is transmitted by *Pediculus humanus*, the human body louse. The organisms are excreted in the faeces of lice and humans acquire the organisms by inoculation when bite sites are scratched. This disease is typically associated with conditions of poor hygiene and overcrowding which promotes person to person spread of the body louse.<sup>5</sup> Rodents are the reservoirs of *Rickettsia typhi* which is transmitted by *Xenopsylla cheopis*, the rat flea via inoculation of faeces. Endemic typhus, also known as Murine typhus, is found in many parts of the world in urban areas with an abundance of rats.<sup>5</sup>

### **Spotted fever group (SFG)**

Organisms belonging to this group are transmitted by ticks, except for *Rickettsia akari*, which is transmitted by mites and *Rickettsia felis* which is transmitted by fleas. The main vector for the transmission of spotted fever is ticks of the family *Ixodidae*. Tick – rickettsia interactions depend on the species of *Rickettsia*. Some *Rickettsia* species can be transmitted by only one species of ticks, whereas others may be transmitted by several tick species, either of the same genus or several different genera. How ticks acquire the organisms is still being debated, with the role of small mammals as reservoirs, co-feeding and sexual transmission being possible routes. However, transovarial passage of organisms clearly plays a role in the maintenance of rickettsiae within the tick population.<sup>6</sup>

Spotted fever group of rickettsiae include traditionally recognized pathogens, organisms recently recognized as being pathogenic and rickettsiae that have only been isolated from ticks. Prototype organisms of the spotted fever group are *Rickettsia rickettsii*, the causative agent of Rocky Mountain spotted fever and *Rickettsia conorii*, the causative agent of Mediterranean spotted fever. *Rickettsia japonica*, *Rickettsia africae*, *Rickettsia honei* and *Rickettsia slovaca* are some of the newer pathogenic rickettsiae belonging to the Spotted fever group.<sup>6</sup> The geographical distribution of spotted fever depends on the distribution of the vector.

### **Scrub typhus**

Scrub typhus, also known as tsutsugamushi disease and chigger borne typhus, is caused by *Orientia tsutsugamushi*. The larval or chigger stages of mites belonging to the genus *Leptotrombidium* are the primary vectors. In addition to being the vector, these mites also act as the natural reservoir for *Orientia tsutsugamushi* by maintaining the organism in nature transovarially and vertically. Scrub typhus is endemic in the Asia Pacific region and found associated with scrub jungles where grass of the Imperata family provides a niche for the mites.<sup>7</sup> *Orientia tsutsugamushi* has over 20 types of distinct antigenic strains, of which Gilliam, Kato and Karp were the initially characterized strains.<sup>7</sup> Recently, a novel *Orientia*

species, *Orientia chuto*, has been described from a patient in Dubai and from mites in Kenya, indicating the possibility of becoming an emerging pathogen.<sup>8,9</sup>

### **Other Rickettsioses**

In addition to the above three groups of diseases, human ehrlichiosis and anaplasmosis, and Q fever caused by *Coxiella burnetii* are also frequently included under the term rickettsioses.

### **Rickettsioses in Sri Lanka**

#### **Earlier literature of rickettsioses in Sri Lanka**

There are reports of outbreaks of scrub typhus among allied soldiers stationed in Ceylon during the world wars.<sup>10,11</sup> Two cases of murine typhus have been reported from Sri Lanka as far back as 1938 (Wijerama, 1930 and Fernando 1938 as quoted by Vasanthathilaka and Senanayake, 1995).<sup>12</sup> In a study conducted in 1972, the seropositivity of antibodies against scrub typhus detected by immunofluorescence assay (IFA) was found to be 6% among hospitalized patients, medical students and blood donors. This population was from the Western Province and the authors concluded that scrub typhus is unlikely to be of major public health concern.<sup>13</sup> Subsequently, a seroprevalence study among animals in Sri Lanka found 20% sero-positivity for *Rickettsia conorii* among goats and 30% sero-positivity among cattle.<sup>14</sup> Vasanthathilaka and Senanayake in 1995 reported a series of cases from Teaching Hospital, Peradeniya, where the diagnosis was made as endemic typhus using the Weil Felix test.<sup>12</sup>

#### **Reports from post 2000s**

More epidemiological data became available from Sri Lanka in the 21<sup>st</sup> century, after local researchers started collaborative work with different international groups, including Centers for Disease Control and Prevention (CDC), Atlanta (USA) and Unite´ des Rickettsies, Marseille, France. Scrub typhus, spotted fever group rickettsioses, endemic typhus and Q fever have been demonstrated in Sri Lanka.<sup>15,16,17</sup>

#### **Geographical distribution of rickettsioses in Sri Lanka**

Geographical distribution of rickettsioses in Sri Lanka is varied and is possibly associated with the distribution of vectors and reservoir animals.

The Central Province has reported a predominance of spotted fever rickettsioses. Distribution of spotted fever rickettsioses in the Central Province was mainly found in the western slopes of the central hills such as Kegalle, Mawanella and the northern parts of the province, up to

Nawalapitiya, Mawanella, Kegalle, Gampola and Nawalapitiya hospitals as well as the major tertiary care centre for these areas, Teaching Hospital, Peradeniya has a regular influx of patients with rickettsioses.<sup>15,17,18,19,20</sup> Serological evidence of scrub typhus and murine typhus has also been reported to a lower extent.<sup>15,19</sup>

The Western Province has predominantly reported patients with scrub typhus, while serological evidence for spotted fever has also been present.<sup>16</sup>

The Southern Province has a mix of rickettsioses. A hospital based study conducted in District General Hospital, Matara in 2009 identified 25 (14%) patients with scrub typhus, 6 (3%) with SFG rickettsioses, 3 (1.6%) with acute Q fever, 3 (1.6%) with murine typhus and 3 (1.6%) infected by *Rickettsia felis*.<sup>21</sup> A study conducted at Teaching Hospital, Karapitiya where 883 paired sera were analyzed, identified 17.7% with confirmed rickettsioses. Spotted fever was the most common type of rickettsioses identified in this study.<sup>22</sup>

The North Western Province predominantly has scrub typhus, as reported by serological evidence from patients admitted to Provincial General Hospital, Kurunegala and Base Hospital, Dambadeniya.<sup>18,23</sup>

The North Central Province has been traditionally linked with scrub typhus. In an island wide surveillance study that used IFA and ELISA as testing methods, patients admitted to Provincial General Hospital, Anuradhapura were identified to have predominantly scrub typhus.<sup>18</sup>

The Northern Province has a predominance of scrub typhus.<sup>24</sup> However, an outbreak attributed to spotted fever, diagnosed by sero-positivity to *Rickettsia conorii* using IFA has been reported from army personnel within the Kilinochchi area from October to December 2012.<sup>25</sup> Premaratne *et al* reported that while scrub typhus was the predominant rickettsioses found among army personnel deployed in the Northern Province presenting with an acute febrile illness, the majority of apparently healthy army personnel had serological evidence of exposure to spotted fever.<sup>26</sup>

Sero-prevalence of rickettsioses among the community has not been studied that well in Sri Lanka. In a study conducted involving healthy volunteers from Kandy, a suburb of Mawanella (Hemmathagama), Mahiyanganaya and Tissa-Kataragama, sero-positivity as defined by an IFA titre of  $\geq 1/64$  has been reported for both *R. conorii* and *O. tsutsugamushi* in all areas.<sup>27</sup>

The studies mentioned above used different testing methods, including IFA and ELISA. Most studies were from single hospitals or included a number of hospitals with voluntary participation. Further, the cut off points used in different studies were different and a single

study including all provinces and districts in a systematic manner has not been conducted in Sri Lanka.

### **Rickettsioses in travellers returning from Sri Lanka**

Sri Lanka is a prime travel destination currently. The demography of travelers arriving in Sri Lanka varies and many of them are engaged in outdoor activities that increase their risk of being bitten by ticks and mites. Rickettsial infections in returning travelers have been reported from France, Norway and Australia.<sup>28,29,30</sup> This is also an issue for Sri Lankans domiciled abroad who return after visiting relatives.<sup>29</sup> In some instances, there have been delays in diagnosing this infective disease. However, as more epidemiological studies and case reports emerge from Sri Lanka, the global community will become aware of Sri Lanka as a hot-spot for rickettsioses and these delays in diagnosis could be minimized.

### **Potential pathogens causing rickettsioses in Sri Lanka**

Identification of the aetiological agent with serology remains problematic due to the high cross reactivity of antibodies. Isolation of the organism in cell cultures or molecular identification is needed for this purpose. Only a few studies have attempted to identify the aetiological agent causing rickettsioses in Sri Lanka using these methods.

*Orientia tsutsugamushi* strains found from patients in Sri Lanka have identified the presence of all major genotypes. This study was conducted using PCR followed by sequencing of the 56kD protein gene present in eschar and buffy coat samples of patients. Karp [Thai-related] genotypes were the most frequent followed by Kato-related, Kawasaki-related and Gilliam-related genotypes. The authors also noted a close homology of one strain with the Kuroki-Boryong organism. This work highlights the diversity of the *Orientia tsutsugamushi* strains in Sri Lanka.<sup>31</sup>

*Rickettsia sibirica mongolitimonae* has been demonstrated in a tissue sample obtained from an eschar using sequencing of the *ompA* gene from a traveler returning to France following a visit to Sri Lanka.<sup>28</sup>

There has also been a report where the species identified from Sri Lanka was found to be most similar to *Candidatus Rickettsia kellyi*, previously reported from Tamil Nadu, India.<sup>32</sup>

However, this remains a research priority for the country as identification of the exact aetiology or aetiologies causing rickettsioses in Sri Lanka will enable implementation of specific control measures as well as to develop more specific diagnostic tests.

## **Clinical presentation of rickettsioses**

Rickettsial infections are traditionally considered to be fevers with rashes with an inoculation eschar. However, presentation of rickettsioses can be non-specific with a wide range of clinical symptoms, which makes it difficult to distinguish this infection clinically from other common viral illnesses.<sup>22</sup> This has been reported in Sri Lanka during an outbreak of chikungunya infections.<sup>33</sup>

In studies conducted in Sri Lanka, inoculation eschar has been mostly associated with scrub typhus.<sup>21</sup> The proportion of patients with confirmed scrub typhus with eschar ranged from 25% to 89%.<sup>16,21,23</sup> Rash is generally associated with a lesser proportion of patients with scrub typhus, sometimes being absent.<sup>21,23</sup>

Spotted fever rickettsioses in Sri Lanka presents predominantly with fever and rash. The proportion of patients with spotted fever presenting with rash has varied from 16% to 100%.<sup>21,34</sup> Eschar is rarely associated with spotted fever.<sup>18,21,24</sup> However, in the outbreak of rickettsioses in the Kilinochchi area mentioned above, a considerable proportion of patients with serological evidence of spotted fever had demonstrated an eschar like lesion, particularly in the eye.<sup>25</sup>

The rash in spotted fever is typically a macular papular rash. In a study conducted at Teaching Hospital, Peradeniya, including 134 patients with serum IgG >1/256 and IgM 1/32, the commonest type of rash identified was a discrete macular papular rash of erythematous hue involving the arms and forearms. Involvement of palms and soles had been noted in about 50% of the study group.<sup>34</sup> Variations in the skin involvement has been described in Sri Lanka, and it is important for treating clinicians to be aware of these differences in order to initiate prompt treatment. Alternative types of rashes that have been reported include fern-leaf pattern skin necrosis<sup>35</sup> and purpura fulminans.<sup>36</sup>

Neurological manifestations may also be associated with rickettsioses. This has been reported in Sri Lanka in association with spotted fever and scrub typhus. Neurological signs in patients with spotted fever have been particularly present among elderly patients. The reported neurological features range from altered consciousness, tremors, rigidity and dyskinesia. According to Kularatne et al, most of the features resolved after treatment with appropriate antibiotics. The authors also state that EEG changes compatible with encephalitis was noted among some patients.<sup>37</sup> Extra pyramidal involvement maybe marked enough to make the presentation very similar to Parkinsonism.<sup>38</sup> Another neurological manifestation that has been attributed to rickettsial infections is facial nerve palsy following intra-aural tick bites.<sup>39</sup>

Joint involvement leads to many patients presenting with joint pains of large and small joints. This has been reported from patients with spotted fever rickettsioses.<sup>20</sup> Patients who present with predominant features of joint involvement, particularly with major joint arthritis have also been reported.<sup>40</sup> Patients with small joint involvement and other features such as oral ulceration and hair loss may lead to an initial impression of connective tissue disorders.<sup>41</sup>

Atypical presentations and complications have been reported among patients with scrub typhus too. Scrub typhus implicated in acute hearing loss has been reported from the Western Province.<sup>42</sup> Patients with scrub typhus presenting with fever and late onset diarrhoea mimicking enteric fever have also been reported.<sup>43</sup> Pancytopenia secondary to haemophagocytosis has also been reported.<sup>44</sup>

### **Association with climate and weather conditions**

An overview of rickettsioses in Sri Lanka shows that the dry regions of the country with scrub jungles has a predominance of scrub typhus while the hilly areas have a predominance of spotted fever.<sup>18</sup> However, exceptions to this has also been reported.

In the North Western Province, the number of cases identified has been higher during the dry season.<sup>23</sup> This may be associated with the seasonal variations of vector density, or behavioral changes associated with the dry season that increases vector human contact. However, a study conducted at the Teaching Hospital, Karapitiya has identified that more patients present during the rainy season.<sup>22</sup> These differences may be due to the behavioral traits of the associated vectors.

### **Vectors and host animals**

While the exact host animals or vectors have not been pinpointed in Sri Lanka, serological evidence for rickettsioses has been found among domestic and wild animals in the country. Most patients with serological evidence of rickettsial infections have association with domestic or wild animals and report contact with potential vectors such as ticks.<sup>20</sup>

Goat and cattle sera obtained from Sri Lanka have been shown to contain antibodies against spotted fever group rickettsial agents, including *Rickettsia conorii*, in addition to antibodies against *Coxiella burnetti*.<sup>45</sup> More recently, serological evidence for exposure to *R. conorii* and *Orientia tsutsugamushi* has been identified among dogs from Kandy, Thambavita, western slope of central hills and Unawatuna, with areas from the western slopes of central hills demonstrating the highest rate of sero-prevalence.<sup>46</sup> Small mammals, namely *Rattus rattus*, *Bandicota indica* and *Mus fernandoni*, captured from Kandy and Kurunegala districts have been identified to have rickettsiae in their blood using qPCR.<sup>47</sup>

Ticks of the *Rhipicephalus* species removed from a patient with demonstrable sero conversion to rickettsial antibodies has been shown to have rickettsial DNA.<sup>39</sup> A number of ticks associated with rickettsial infections have been recovered from both humans (autocariasis) and animals in Sri Lanka. Interestingly, these ticks are known to reside on domestic as well as wild animals.<sup>48</sup> PCR based testing for 17 kDa antigen of spotted fever rickettsiae has identified these to be present in ticks found on animals in Sri Lanka. These have been found in three *Amblyomma* species: *Amblyomma testudinairum* found on a wild boar, *Amblyomma clypeolatum* found on a star tortoise, and *Amblyomma javanense* found on a pangolin and *Rhipicephalus sanguineus* found on a dog.<sup>48</sup> All species except *A. javanense* have been known to infect humans and therefore can contribute to the spread of rickettsioses in Sri Lanka.

Ectoparasites present on *Suncus murinus*, *Bandicota indica* and *Golunda ellioti*, captured from Kurunegala and Kandy districts have demonstrated to have rickettsiae. These ectoparasites included *Rhipicephalus haemaphysaloides*, *Ixodes ceylonensis*, *Haemaphysalis spinigera*, *Haemaphysalis sp.*, *Stivalius aporus* and *Xenopsylla cheopes*.<sup>47</sup> Japanese researchers have identified rickettsiae in *Amblyomma trimaculatum* ticks found as ecto-parasites on snakes (*Boiga forsteni*) from Sri Lanka.<sup>49</sup>

### **Potential for further research and development**

Rickettsioses are a group of notifiable diseases in Sri Lanka. However, most patients are diagnosed on clinical suspicion, and in the absence of laboratory confirmation, identification of the actual disease burden is problematic.

Sri Lanka does not have sufficient laboratory facilities to cater to all hospitals that treat patients with rickettsioses. Clinicians in regions where rickettsioses are endemic commence treatment with appropriate antibiotics on clinical suspicion. In a study conducted on 28 febrile patients, after 7 days of hospitalization without a confirmed diagnosis and who responded rapidly to doxycycline, 21 had shown serological evidence of rickettsioses.<sup>50</sup>

While use of paired sera to demonstrate a rise in antibody titre is the gold standard for diagnosis of rickettsioses, it is practically difficult in clinical settings. Establishment of a cut off value to interpret a single antibody titre detected by IFA is also a research priority. Using a cut off level of >1/256 for IgG for diagnosis of spotted fever has been associated with a false positive rate of 11.3% and a false negative rate of 4.3% among those with illness for > 7 days. The same cut off has been associated with a 0% false positive rate and a 12% false negative rate among those with illness for < 7 days. For scrub typhus, the same cut off has had a false positive rate of 2% and a false negative rate of 0% among those with illness for > 7 days, and a false positive rate of 0% and a false negative rate of 14.2% among those with illness for < 7 days.<sup>51</sup> However, these values need to be regionally validated. This is difficult in the context of

high seroprevalence among healthy individuals.<sup>27</sup> Locally validated algorithms including clinical features, IFA titres as well as duration of illness may be the way forward.

The increasing interaction of wild animals such as monkeys, peacocks and wild boar with domestic animals and humans may lead to an increase in rickettsial infections.<sup>48</sup> Mapping out the ecological niche of vectors and hosts of rickettsial infections is also a need.

While there have been remarkable improvements in rickettsiology in Sri Lanka during the past decade, much remains to be elucidated. A comprehensive approach involving public health officials, veterinarians, medical doctors, zoologists and environmentalists with a one health approach is essential for the further development of the field.

## References

1. Walker DH. Rickettsiae and rickettsial infections: the current state of knowledge. *Clin Infect Dis.* 2007; 45 (Suppl 1):S39-44. doi: <https://doi.org/10.1086/518145>
2. La Scola B, Raoult D. Laboratory diagnosis of rickettsioses: current approaches to diagnosis of old and new rickettsial diseases. *J Clin Microbiol.* 1997; 35(11):2715-27. Review. PubMed PMID: 9350721; PMCID:PMC 230049.
3. Faccini-Martínez AA, García-Álvarez L, Hidalgo M, Oteo JA. Syndromic classification of rickettsioses: an approach for clinical practice. *Int J Infect Dis.* 2014; 28:126-39. doi: [10.1016/j.ijid.2014.05.025](https://doi.org/10.1016/j.ijid.2014.05.025).
4. Portillo A, Santibáñez S, García-Álvarez L, et al. Rickettsioses in Europe. *Microbes Infect.* 2015; 17(11-12):834-8. doi: [10.1016/j.micinf.2015.09.009](https://doi.org/10.1016/j.micinf.2015.09.009).
5. Raoult D, Roux V. Rickettsioses as paradigms of new or emerging infectious diseases. *Clin Microbiol Rev.* 1997; 10(4):694-719. doi: <https://doi.org/10.1128/CMR.10.4.694>
6. Parola P, Paddock CD, Raoult D. Tick-borne rickettsioses around the world: emerging diseases challenging old concepts. *Clin Microbiol Rev.* 2005; 18(4):719-56 doi: <https://doi.org/10.1128/CMR.18.4.719-756.2005>
7. Kelly DJ, Fuerst PA, Ching WM, Richards AL. Scrub typhus: the geographic distribution of phenotypic and genotypic variants of *Orientia tsutsugamushi*. *Clin Infect Dis.* 2009; 15;48 (Suppl 3):S203-30. doi: <https://doi.org/10.1086/596576>
8. Izzard L, Fuller A, Blacksell SD, et al. Isolation of a novel *Orientia* species (*O. chuto* sp. nov.) from a patient infected in Dubai. *J Clin Microbiol.* 2010; 48(12):4404-9. doi: [10.1128/JCM.01526-10](https://doi.org/10.1128/JCM.01526-10).
9. Masakhwe C, Linsuwanon P, Kimita G, et al. Identification and characterization of *Orientia chuto* in trombiculid chigger mites collected from wild rodents in Kenya. *J Clin Microbiol.* 2018; 56(12):e0 1124-18. doi:[10.1128/JCM.01124-18](https://doi.org/10.1128/JCM.01124-18).
10. Kelly DJ, Richards AL, Temenak J, et al. The past and present threat of rickettsial diseases to military medicine and international public health. *Clin Infect Dis.* 2002 15;34(Suppl 4):S145-69. doi: <https://doi.org/10.1086/339908>
11. Premaratne. Ranjan. Rickettsial infections in Sri Lanka: yesterday, today, tomorrow. P.B. Fernando Oration 2010. *Journal of the Ceylon College of Physicians.* 2011; 42:11-15

No doi

12. Vasanthathilaka VWJK, Senanayake N. Typhus fever from the mountainous areas in Central Sri Lanka. *Kandy Medical Journal*.1999; 5:4:6-9. No doi
13. Van Peenen PF, See R, Soysa PE, Irving GS. Sero-epidemiological survey of hospital-associated populations in Colombo, Sri Lanka. *Southeast Asian J Trop Med Public Health*. 1976; 1:16-20. No doi
14. Kováčová E, Sixl W, Stünzner D, et al. Serological examination of human and animal sera from six countries of three continents for the presence of rickettsial antibodies. *Eur J Epidemiol*. 1996; 12(1):85-9. doi: <http://dx.doi.org/10.1007/BF00144434>
15. Kularatne SAM, Edirisingha JS, Gawarammana IB, et al. Emerging rickettsial infections in Sri Lanka: the pattern in the hilly Central Province. *Trop Med Int Health*. 2003; 8(9):803-11. doi: <https://doi.org/10.1046/j.1365-3156.2003.01108.x>
16. Premaratna R, Loftis AD, Chandrasena TG, et al. Rickettsial infections and their clinical presentations in the Western Province of Sri Lanka: a hospital-based study. *Int J Infect Dis*. 2008; 12(2):198-202. doi: <https://doi.org/10.1016/j.ijid.2007.06.009>
17. Nagalingam K, Rolain JM, Thevanesam V, et al. Spotted fever rickettsioses in children in Sri Lanka. *Clin Microbiol Infect*. 2009; 15 (Suppl 2):330-1. doi: [10.1111/j.1469-0691.2008.02262.x](https://doi.org/10.1111/j.1469-0691.2008.02262.x).
18. Liyanapathirana VC, Thevanesam V. Seroepidemiology of rickettsioses in Sri Lanka: a patient based study. *BMC Infect Dis*. 2011; 11:328. doi:[10.1186/1471-2334-11-328](https://doi.org/10.1186/1471-2334-11-328).
19. Kularatne SAM, Rajapakse RP, Wickramasinghe WM, et al. Rickettsioses in the central hills of Sri Lanka: serological evidence of increasing burden of spotted fever group. *Int J Infect Dis*. 2013; 17(11):e988-92. doi: [10.1016/j.ijid.2013.05.014](https://doi.org/10.1016/j.ijid.2013.05.014).
20. Weerakoon KG, Kularatne SAM, Rajapakse J, et al. Revisiting clinico-epidemiological pattern of human rickettsial infections in the central region of Sri Lanka: a hospital based descriptive study. *BMC Res Notes*. 2017; 10(1):400. doi: [10.1186/s13104-017-2727-1](https://doi.org/10.1186/s13104-017-2727-1).
21. Angelakis E, Munasinghe A, Yaddehige I. Detection of rickettsioses and Q fever in Sri Lanka. *Am J Trop Med Hyg*. 2012; 86(4):711-2. doi: [10.4269/ajtmh.2012.11-0424](https://doi.org/10.4269/ajtmh.2012.11-0424).
22. Reller ME, Bodinayake C, Nagahawatte A, et al. Unsuspected rickettsioses among patients with acute febrile illness, Sri Lanka, 2007. *Emerg Infect Dis*. 2012; 18(5):825-9. doi: [10.3201/eid1805.111563](https://doi.org/10.3201/eid1805.111563).
23. De Silva N, Wijesundara S, Liyanapathirana V, et al. Scrub typhus among pediatric patients in Dambadeniya: a base hospital in Sri Lanka. *Am J Trop Med Hyg*. 2012; 87(2):342-4. doi: [10.4269/ajtmh.2012.12-0170](https://doi.org/10.4269/ajtmh.2012.12-0170).
24. Pradeepan JA, Ketheesan N, Murugananthan K. Emerging scrub typhus infection in the northern region of Sri Lanka. *BMC Res Notes*. 2014; 7:719. doi:[10.1186/1756-0500-7-719](https://doi.org/10.1186/1756-0500-7-719).
25. Dahanayaka N.J., Semage S.N., Weerakoon K.G.,. An unusual outbreak of Rickettsial infection among army soldiers engaged in reconnaissance mission in Northern Sri Lanka. *Ceylon Medical Journal* 2017; 62(2), pp.108–109. doi: <http://doi.org/10.4038/cmj.v62i2.8477>
26. Premaratna R, Ariyaratna N, Attanayake C, et al. Rickettsial infection among military personnel deployed in Northern Sri Lanka. *BMC Infect Dis*. 2014; 14:3864. doi: [10.1186/s12879-014-0688-8](https://doi.org/10.1186/s12879-014-0688-8)

27. Nanayakkara DM, Kularatne SAM, Wickramasingh WMRS,. Seroprevelence of rickettsioses among human population of Sri Lanka: A study in four regions. *Proceedings of the Peradeniya University Research Sessions, Sri Lanka*. 2009; 14:65–67.  
Available at <http://dlib.pdn.ac.lk/handle/1/4438>. Accessed on 28/12/2018
28. Cordier, C., P. Tattevin, C. Leyer, M. et al. “Rickettsia Sibirica Mongolitimonae Infection, Sri Lanka”. *The Journal of Infection in Developing Countries*. 2017; 11(08):668-71.  
doi: <https://doi.org/10.3855/jidc.8743>
29. Jensenius M, Montelius R, Berild D, Vene S. Scrub typhus imported to Scandinavia. *Scand J Infect Dis*. 2006; 38(3):200-2. doi: <https://doi.org/10.1080/00365540500277342>
30. Stokes PH, Walters BJ. Spotted fever rickettsiosis infection in a traveler from Sri Lanka. *J Travel Med*. 2009; 16(6):436-8. doi: [10.1111/j.1708-8305.2009.00360.x](https://doi.org/10.1111/j.1708-8305.2009.00360.x).
31. Premaratna R, Blanton LS, Samaraweera DN, et al. Genotypic characterization of *Orientia tsutsugamushi* from patients in two geographical locations in Sri Lanka. *BMC Infect Dis*. 2017; 17(1):67. doi: [10.1186/s12879-016-2165-z](https://doi.org/10.1186/s12879-016-2165-z).
32. Nanayakkara DM, Serological detection and identification of Rickettsial species infecting humans. MPhil Thesis. Postgraduate Institute of Science, University of Peradeniya, Sri Lanka. 2011. Available from  
<http://dlib.pdn.ac.lk/bitstream/123456789/2973/1/Nanayakkara%202011.pdf>. Last accessed on 31/12/2018.
33. Premaratna R, Halambarachchige LP, Nanayakkara DM, et al. Evidence of acute rickettsioses among patients presumed to have chikungunya fever during the chikungunya outbreak in Sri Lanka. *Int J Infect Dis*. 2011; 15(12):e871-3. doi: [10.1016/j.ijid.2011.09.010](https://doi.org/10.1016/j.ijid.2011.09.010).
34. Weerakoon K, Kularatne SA, Rajapakse J, et al. Cutaneous manifestations of spotted fever rickettsial infections in the Central Province of Sri Lanka: a descriptive study. *PLoS Negl Trop Dis*. 2014; 8(9):e3179. doi: [10.1371/journal.pntd.0003179](https://doi.org/10.1371/journal.pntd.0003179).
35. Luke N, Munasinghe H, Balasooriya L, Premaratna R. Widespread subcutaneous necrosis in spotted fever group rickettsioses from the coastal belt of Sri Lanka- a case report. *BMC Infect Dis*. 2017; 17(1):278. doi: [10.1186/s12879-017-2375-z](https://doi.org/10.1186/s12879-017-2375-z).
36. Dalugama C, Gawarammana IB. Rare presentation of rickettsial infection as purpura fulminans: a case report. *J Med Case Rep*. 2018; 12(1):145. doi: [10.1186/s13256-018-1672-5](https://doi.org/10.1186/s13256-018-1672-5).
37. Kularatne SAM, Weerakoon KG, Rajapakse RP, et al A case series of spotted fever rickettsiosis with neurological manifestations in Sri Lanka. *Int J Infect Dis*. 2012 ;16(7):e514-7. doi: [10.1016/j.ijid.2012.02.016](https://doi.org/10.1016/j.ijid.2012.02.016).
38. Premaratna R, Wijayalath SH, Miththinda JK,. Scrub typhus mimicking Parkinson's disease. *BMC Res Notes*. 2015; 8:438. doi: [10.1186/s13104-015-1428-x](https://doi.org/10.1186/s13104-015-1428-x).
39. Kularatne SAM, Fernando R, Selvaratnam S, et al. Intra-aural tick bite causing unilateral facial nerve palsy in 29 cases over 16 years in Kandy, Sri Lanka: is rickettsial aetiology possible? *BMC Infect Dis*. 2018; 18(1):418. doi: [10.1186/s12879-018-3338-8](https://doi.org/10.1186/s12879-018-3338-8).
40. Premaratna R, Chandrasena TG, Rajapakse RP,. Rickettsioses presenting as major joint arthritis and erythema nodosum: description of four patients. *Clin Rheumatol*. 2009; 28(7):867-8. doi: [10.1007/s10067-009-1166-3](https://doi.org/10.1007/s10067-009-1166-3).
41. Premaratna R, Liyanarachchi E, Rajapakse R, et al. A patient with spotted fever group rickettsiosis mimicking connective tissue disease. *Ceylon Medical Journal*. 2012;57(3):127–128. doi: <http://doi.org/10.4038/cmj.v57i3.4707>

42. Premaratna R, Chandrasena TG, Dassayake AS, et al. Acute hearing loss due to scrub typhus: a forgotten complication of a reemerging disease. *Clin Infect Dis*. 2006; 42(1):e6-8. doi: <https://doi.org/10.1086/498747>
43. Premaratna R, Nawasiwatte BM, Niriella MA, et al. Scrub typhus mimicking enteric fever; a report of three patients. *Trans R Soc Trop Med Hyg*. 2010; 104(4):309-10. doi: [10.1016/j.trstmh.2009.08.011](https://doi.org/10.1016/j.trstmh.2009.08.011)
44. Premaratna R, Williams HS, Chandrasena TG, et al. Unusual pancytopenia secondary to haemophagocytosis syndrome in rickettsioses. *Trans R Soc Trop Med Hyg*. 2009; 103(9):961-3. doi: [10.1016/j.trstmh.2009.04.003](https://doi.org/10.1016/j.trstmh.2009.04.003)
45. Kováčová E, Sixl W, Stünzner D, Urvölgyi J, Kazár J. Serological examination of human and animal sera from six countries of three continents for the presence of rickettsial antibodies. *Eur J Epidemiol*. 1996;12(1):85-9. No doi
46. Nanayakkara DM, Rajapakse RP, Wickramasinghe S, Kularatne SA. Serological evidence for exposure of dogs to *Rickettsia conorii*, *Rickettsia typhi*, and *Orientia tsutsugamushi* in Sri Lanka. *Vector Borne Zoonotic Dis*. 2013; 13(8):545-9. doi: [10.1089/vbz.2012.1049](https://doi.org/10.1089/vbz.2012.1049)
47. Yathramullage S, Rajapakse J, Boyagoda S. Rickettsiae reservoirs among small mammals (rats, mice and shrews) and their arthropod vectors in Sri Lanka. *Ceylon Journal of Science*. 2018; 47(2):175–183. doi: <http://doi.org/10.4038/cjs.v47i2.7514>
48. Liyanaarachchi DR, Rajakaruna RS, Dikkumbura AW, Rajapakse RP. Ticks infesting wild and domestic animals and humans of Sri Lanka with new host records. *Acta Trop*. 2015; 142:64-70. doi: [10.1016/j.actatropica.2014.11.001](https://doi.org/10.1016/j.actatropica.2014.11.001)
49. Andoh M, Sakata A, Takano A, et al. Detection of *Rickettsia* and *Ehrlichia* spp. in ticks associated with exotic reptiles and amphibians imported into Japan. *PLoS One*. 2015; 10(7):e0133700. doi: [10.1371/journal.pone.0133700](https://doi.org/10.1371/journal.pone.0133700)
50. Premaratna R, Rajapakse RP, Chandrasena TG, et al. Contribution of rickettsioses in Sri Lankan patients with fever who responded to empirical doxycycline treatment. *Trans R Soc Trop Med Hyg*. 2010; 104(5):368-70. doi: [10.1016/j.trstmh.2009.10.006](https://doi.org/10.1016/j.trstmh.2009.10.006)
51. Premaratna R, Weerasinghe S, Ranaweera A, et al. Clinically helpful rickettsial disease diagnostic IgG titers in relation to duration of illness in an endemic setting in Sri Lanka. *BMC Res Notes*. 2012; 5:662. doi: [10.1186/1756-0500-5-662](https://doi.org/10.1186/1756-0500-5-662)