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Short Report: Scrub Typhus among Pediatric Patients in Dambadeniya: A Base Hospital in Sri Lanka

Nalika De Silva, Sarojini Wijesundara, Veranja Liyanapathirana,* Vasanthi Thevanesam, and John Stenos

Paediatric Unit, Base Hospital, Dambadeniya, Sri Lanka; Department of Microbiology, Faculty of Medicine, University of Peradeniya, Peradeniya, Sri Lanka; Australian Rickettsial Reference Laboratory, Barwon Health, Geelong, Australia

Abstract. Data on pediatric scrub typhus is uncommon in Sri Lanka and other countries. The objective of this study was to identify the clinical features of patients with scrub typhus at a Base Hospital in Sri Lanka. Sixty patients presenting with suspected scrub typhus were included in the study. Their blood samples were tested for the presence of antibodies against rickettsioses using the reference method. Twenty patients had confirmed scrub typhus and 24 had possible scrub typhus. Their clinical features are discussed in this work.

INTRODUCTION

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi* (formerly *Rickettsia*).[1] An estimated one million cases occur annually and as many as one billion people living in endemic areas may have been infected at some time.

Orientia tsutsugamushi is an obligate intracellular gram-negative bacterium that lives in trombiculid mites (Species: *Leptotrombidium*)—the primary vector. Mites feed on rodents that act as reservoirs for this agent. *Orientia tsutsugamushi* is transmitted to humans mainly through the bite of an infected chigger, the larval stage of the mite.

Proliferation of the bacterium occurs at the site, forming a characteristic skin lesion known as an eschar. After an incubation period of 6–21 days, the symptoms of high fever (40°C) with chills, headache, cutaneous rash, lymphadenopathy, cough, myalgia, and anorexia occur. Complications such as meningitis and pneumonitis following scrub typhus have been reported.[1,2]

Although serologic surveys suggest that as many as one-fourth of cases of scrub typhus might occur in children, very few reports of childhood scrub typhus are available in the medical literature.[2]

Several outbreaks of rickettsial infections have been reported from Sri Lanka in the recent past. In the low country, the most common type is reported to be Scrub typhus.[3] A study on adult patients in the Central Province showed the presence of different types of rickettsial infections including *O. tsutsugamushi*, *Rickettsiae typhi*, and spotted fever group species.[4] Another study done in children from the Central Province identified spotted fever group rickettsiosis to be the common agent and did not report a single child with scrub typhus.[5]

The Weil–Felix test, which is commonly used in Sri Lanka, is non-specific and not useful in making a diagnosis of scrub typhus. Indirect fluorescent antibody assay (IFA), which is the more accurate method of diagnosing rickettsial infection is available only at a few centers in Sri Lanka. Therefore, treatment is based mainly on a clinical diagnosis.

The objective of this study was to identify the clinical features of patients presenting to a Base Hospital in Sri Lanka with scrub typhus.

*Address correspondence to Veranja Liyanapathirana, Department of Microbiology, Faculty of Medicine, University of Peradeniya, 0777060887. E-mail: veranjacl@yahoo.com

METHOD

Study population. Serum samples of patients with possible scrub typhus presenting to Base Hospital, Dambadeniya, a Base Hospital in the North Western Province of Sri Lanka from August 2009 to December 2010 were sent for confirmation to the Department of Microbiology, Faculty of Medicine, University of Peradeniya as a part of an island-wide surveillance program conducted with human ethics approval, given by the university. Patients who had fever with chills for more than 7 days with either a history of a tick/mite bite or an eschar or both were included in the study, and they were observed for the presence of lymphadenopathy, splenomegaly, hepatomegaly, and thrombocytopenia. A few patients who had fever with chills for more than 7 days with neither history of tick bite nor an eschar, however associated with one or a combination of the latter clinical signs, were also considered as possibly having rickettsial infections based on clinical judgment. All patients admitted to this unit were routinely seen and extensively examined by the principal investigator, and the positive and negative features were documented in the patient notes. The clinical features were subsequently tabulated.

These patients were treated with intravenous (IV) or oral chloramphenicol depending on availability and bled with parental consent. Confirmatory rickettsial testing was performed on the sera posted to the laboratory. Acute and convalescent sera (taken 10–14 days apart) were available in 39 patients and single (acute) samples in the remaining 21 patients.

Serological testing. All sera were tested using an IFA test (donated by the Rickettsial Reference Laboratory, Geelong, Australia) at the Department of Microbiology, Faculty of Medicine, University of Peradeniya. Acute and convalescent samples of a given patient were tested in parallel according to the manufacturer's guidelines.

Interpretation of test results. An IFA titer of ≥ 1of 128 for IgM or IgG was considered as positive. Samples that screened positive for spotted fever were tested subsequently using an antigen panel consisting of *Rickettsia conorii*, *Rickettsia honei*, *Rickettsia siberica*, *Rickettsia australis*, *Rickettsia rickettsii*, and *Rickettsia akari*. Samples that screened positive for scrub typhus were tested against a panel consisting of three serotypes of *O. tsutsugamushi* Gilliam, Karp, and Kato. Typhus group positive sera were screened with a panel consisting of *Rickettsia prowazekii* and *Rickettsia typhi.* All sera were titrated with dilutions ranging from 1 of 128 to 1 of 1024. A 4-fold rise in the antibody titer between the acute and convalescent samples were

TABLE 1
Summary of serology test results

Result category		Number of patients
Patients with 4-fold rise in antibody titer (patients with confirmed scrub typhus).		20
Patients with a titer of 1/1,024 in both acute and convalescent samples.	Patients with possible scrub typhus.	4
Patients with 2-fold rise or seroconversion in antibody titer.		4
Patients in whom a single serum sample was available with a titer of ≥ 1/128 in IgM or IgG.		16
Confirmed serology negative patients (paired sera available).		11
Possible serology negative (negative single sample).		5
Total		60

taken as being confirmatory of rickettsioses. If a sample gave a titer of > 1 of 128 for more than one antigen, interpretation was done as follows. Where there was a ≥ 4-fold difference in titer between the highest and the second highest titer, the antigen against which the highest antibody titer was found was taken as the probable causative agent. In instances where the difference was < 4-fold, mixed antibody positivity was inferred.[6]

RESULTS

Sixty patients were recruited between August 2009 and December 2010. Of these patients, paired sera were available for 39 patients. Patients ranged from 1 to 11 years of age and there were 62% male and 38% female patients.

Patients could be categorized into six groups according to the serological results (Table 1).

All *O. tsutsugamushi* serology positive patients had *O. tsutsugamushi* Gilliam strain as the predominant serotype to which antibodies were found. The remaining sera were negative for the spotted fever group or typhus group infection. The clinical features of the patients are summarized in Table 2.

All patients were treated either with IV or oral chloramphenicol and the response to treatment is summarized in Table 3.

TABLE 2
Clinical data

Clinical features	Patients with confirmed scrub typhus, *N* = 20	Patients with possible scrub typhus, *N* = 24	Confirmed serology negative patients, *N* = 11	Possible serology negative, *N* = 5
Mean duration of fever on presentation (days)	11	9.1	8	8.8
History of tick/mite bites	15 (75%)	17 (70%)	7 (63%)	5 (100%)
Presence of eschar	5 (25%)	10 (41%)	2 (18%)	0
Presence of rash	0	3 (12 %)	1 (9%)	0
Respiratory symptoms of signs	9 (45%)	12 (50%)	5 (45%)	4 (80%)
Lymphadenopathy	12 (60%)	10 (41%)	3 (27%)	2 (40%)
Splenomegaly	7 (35%)	10 (41%)	3 (27%)	1 (20%)
Hepatomegaly	19 (95%)	17 (70%)	8 (72%)	5 (100%)
Platelet count of < 150,000/mL	4 (20%)	7 (29%)	2 (18%)	2 (40%)
Diarrhoea	1 (5%)	0	0	0

TABLE 3
Response to treatment with IV/oral chloramphenicol*

Category of patients	Route of administration	Response within 24 hours	48 hours	72 hours	> 72 hours	Data not available
Patients with confirmed scrub typhus, *N* = 20	IV (n = 13)	11	2	0	0	0
	Oral (n = 7)	0	3	3	1	0
Patients with possible scrub typhus, *N* = 24	IV (n = 20)	10	6	4	0	0
	Oral (n = 4)	0	2	0	1	1
Confirmed serology negative patients, *N* = 11	IV (n = 3)	1	1	1	0	0
	Oral (n = 8)	3	0	3	2	0
Possible serology negative patients, *N* = 5	IV (n = 4)	0	3	1	0	0
	Oral (n = 1)	1	0	0	0	0

*IV = intravenous.

Data with regard to the month of admissions of the patients with confirmed or possible rickettsioses presenting to Base Hospital, Dambadeniya were compared with the data for 2010 for the Kurunegala district, the administrative district to which the hospital belongs (Figure 1) and the rainfall data for Bopitiya, which is the closest (6 km) rainfall collection center to Dambadeniya (Figure 2).

DISCUSSION

The study included 60 patients of whom 20 had serologically confirmed scrub typhus and 24 were possible cases of rickettsioses. Dambadeniya is situated in the North Western province of Sri Lanka and is a predominantly agricultural community with plenty of scrub jungles where vectors for scrub typhus are present. Though the Gilliam strain was found to be the predominant strain among the study population, as the panel of antigens included only Gilliam, Karp, and Kato strains, it is premature to conclude that Gilliam is the predominant strain.

Of the 20 patients with confirmed scrub typhus, 25% had an eschar. Considering the confirmed and possible cases together, eschars were observed in 34% of patients. They were mainly seen on the scrotum, axilla, and neck. The prevalence of

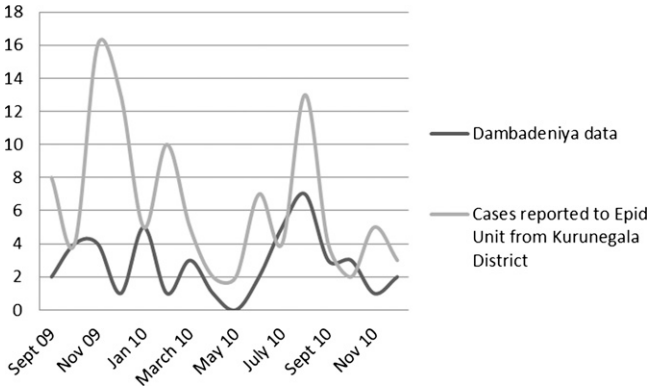

FIGURE 1. Comparison of the number of patients presenting at Base Hospital Dambadeniya with possible or confirmed scrub typhus with that of patients presenting to all hospitals in Kurunegala district with possible rickettsioses as reported by the Epidemiology Unit (Epid Unit), Ministry of Health, Sri Lanka for the same period.

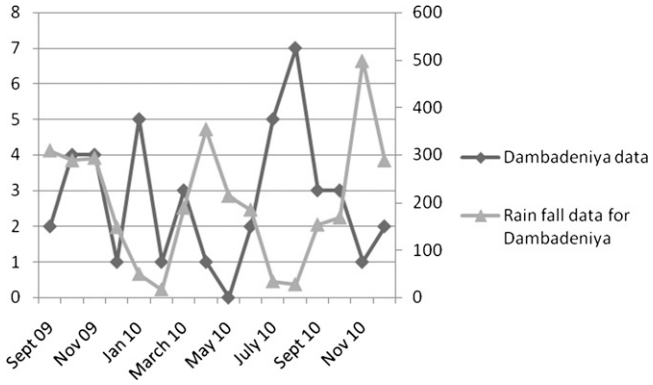

FIGURE 2. Relationship of the number of patients presenting to Base Hospital Dambadeniya with possible or confirmed scrub typhus with local rainfall.

eschars was lower than previously reported in children in Thailand and in Sri Lankan adults.[2,3] However, a lower prevalence of eschar is a known phenomenon in patients with scrub typhus in South Asia, especially those who are dark skinned.[7] The eschars were primarily detected by a medical officer on routine examination and not noted or commented on by the patient or caregiver. This highlights the need for careful examination for eschars by health care professionals.

Although a history of tick/mite bite was noted in 75% of patients with confirmed rickettsiosis, there were instances where an eschar was noted in the absence of a history of tick/mite bite. This could be caused by a lack of awareness of the parents to the presence of ticks/mites and their ability to cause disease in humans. Because scrub typhus is caused by the larval stage of the mite, which is very small,[8] it can be easily missed. The difference between a tick and a mite is also poorly understood by the general public and medical staff.

A rash was not seen in a single patient with confirmed rickettsiosis and only in 2 (12%) with possible infection. This is in keeping with other studies done in the region where a rash was seldom seen in patients with scrub typhus[3] when compared with spotted fever group rickettsioses.[5]

It was observed by the principal investigator that most of the patients were well between febrile episodes, which were a striking feature (data not shown). This characteristic feature has been described in previous studies as well.

Thirty-five percent of patients who had confirmed and possible infection had splenomegaly, which was also a striking feature.

The relatively non-specific clinical features detected in the study emphasize the need for laboratory confirmation of suspected rickettsial infections.

Response to treatment was more rapid when given IV chloramphenicol. In 84.6% of children, the fever responded within 24 hours, whereas not a single patient responded within 24 hours when given oral chloramphenicol. To our knowledge, there is no published data where oral and IV treatment with chloramphenicol have been compared for the treatment of scrub typhus.

Seasonal variation was observed with two peaks in January and August. The peak in August coincides with a peak in the reported number of patients with suspected rickettsioses presenting to hospitals in the Kurunegala district to which Dambadeniya belongs. This is possibly related to changes in rainfall patterns and associated vector activity. Comparison of rainfall data for the region with the number of patients revealed that the highest patient numbers were seen during the dry season, compared with the wet season. This may be caused by the increase in outdoor activities during the dry season leading to more vector exposure, however studies conducted over a longer period of time are needed to establish the persistence of this pattern.

In conclusion, this study raises the awareness of clinicians of the existence of scrub typhus infection, its presentation, and consideration in the differential diagnosis of a child with fever from within the epidemiological boundaries of this area. The wider implications of this in relation to international travel medicine also need to be considered.

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Authors' addresses: Nalika De Silva and Sarojini Wijesundara, Pediatric Unit, Base Hospital, Dambadeniya, Sri Lanka, E-mails: nalikades@yahoo.com and methmalie@yahoo.com. Vasanthi Thevanesam, University of Peradeniya, Department of Microbiology, Peradeniya, Sri Lanka, E-mail: vasanthithevanesam@yahoo.com. John Stenos, Australian Rickettsial Reference Laboratory, Douglas Hocking Research Institute, The Geelong Hospital, Geelong, Victoria, Australia, E-mail: johns@barwonhealth.org.au.

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