Comparison of Preferred Bite Sites between Mites and Ticks on Humans in Korea

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Abstract. Identification of mite and tick bite sites provides important clinical information. The predominant mite species in Korea associated with scrub typhus are *Leptotrombidium pallidum* and *Leptotrombidium scutellare*. The most abundant tick species is *Haemaphysalis longicornis*. To date, there has been no comparative study on preferred bite sites between mites and ticks in humans. This study included a review of medical records and a field study. For mite bite sites, eschars were checked on 506 patients with scrub typhus, confirmed by indirect immunofluorescence assay or nested polymerase chain reaction on the 56-kDa type-specific antigen gene of *Orientia tsutsugamushi*. Tick bite sites were identified and marked on a diagram for 91 patients who experienced tick bites within the previous year through a field epidemiological investigation. The mite and tick bite sites in Koreans were compared. The most frequently observed mite bite sites were the anterior chest, including the axillae (29.1%) and the abdominal region, including the inguinal area (26.1%). Tick bite sites were most frequent on the lower extremities (33.0%), followed by the abdominal region, including the inguinal area (26.4%), and upper extremities (26.4%). The distribution was significantly different between mite and tick bite sites ($P < 0.001$). There was a statistically significant difference in the mite bite ($P = 0.001$), but not tick bite sites ($P = 0.985$), between men and women. This is the first report on the differences between tick and mite bite sites, and may help clinicians reach a rapid diagnosis of mite- or tick-borne infection.

INTRODUCTION

Acaridans are broadly distributed worldwide and have different habits; most live freely but some are parasitic. There are approximately 500,000 acaridan species that are divided into mites and ticks depending on morphological characteristics.¹ Acaridans are vectors of diseases, including viral, rickettsial, and bacterial diseases. Mites are vectors for diseases such as scrub typhus and rickettsialpox. Ticks can transmit the agents of diseases such as Lyme disease, human ehrlichiosis, anaplasmosis, babesiosis, relapsing fever, Rocky Mountain spotted fever, Colorado tick fever, tularemia, Q fever, and tick paralysis.^{2,3} Furthermore, ticks, mites, lice, and fleas are the vectors responsible for all rickettsial diseases in humans.⁴

According to the Korea Centers for Disease Control, the rate of scrub typhus, a mite-borne disease, increased from 2,637 patients in 2001 to 6,780 patients in 2005, and scrub typhus was detected in > 8,000 patients annually from 2012 to 2014. Tick-borne infectious diseases were not detected before 2010 in Korea; however, the first patient with severe fever with thrombocytopenia syndrome (SFTS) was identified in 2013.⁵ The number of patients with SFTS has continuously increased, from 36 patients in 2013 to 55 patients in 2014,⁶ and a patient with anaplasmosis was also reported in Korea in 2013.⁷

The clinical symptoms of scrub typhus include fever, headache, fatigue, myalgia, skin rash, and lymphadenopathy and generally occur after 6- to 18-day latency period post-infection.⁸ The primary mite vectors transmitting *Orientia*

tsutsugamushi include *Leptotrombidium deliense* in southeast Asia; *Leptotrombidium akamushi*, *Leptotrombidium pallidum*, and *Leptotrombidium scutellare* in Japan; and *L. pallidum* and *L. scutellare* in Korea.^{9,10} Chiggers, larvae of the Trombiculidae family of mites that have been infected with *O. tsutsugamushi*, a pathogen in wild rats or wild animals, must consume tissue fluids of vertebrates to metamorphose into the nymph stage. When chiggers bite humans, pathogens enter the skin and cause scrub typhus.^{8,11} Dry, dark, 0.5- to 2-cm eschars surrounded by an erythematous rim are formed at the bite site; these lesions are not pruritic or tender.^{8,12}

An antibody test is used to establish the diagnosis of scrub typhus. However, treatment is usually initiated based on the identification of eschars even before the antibody test results are available. Eschars are one of the most critical findings for diagnosis. Because it takes > 3–4 weeks for eschars to fall off and new healthy skin to form, it is possible to observe eschars for a considerable period.¹³ Polymerase chain reaction (PCR) testing of eschars is more sensitive than that of other tissues; therefore, identifying common eschar sites could enable rapid diagnosis^{14,15} and treatment.¹⁶

Ticks tend to prefer specific hosts, such as vertebrate hosts, including humans, and wild and domestic animals, depending on the species and lifecycle stage. The species and lifecycle stage, as well as host adherence, duration of attachment, location of human activity, and geographical and weather conditions, also affect the spread of tick-borne infectious diseases.^{17,18} In a study by Park and others, a total of 13,053 ticks were collected using flag or drag methods from bushes in the nine provinces of South Korea, and *Haemaphysalis longicornis* was the most abundant species, followed by *Haemaphysalis flava*.¹⁹ In another study, of 261 ticks that bit or adhered to human bodies, 212 (81.2%) *H. longicornis*, 17 (6.5%) *Amblyomma testudinarium*, and 15 (5.7%) *Ixodes nipponensis* were identified.²⁰ Although SFTS is considered to

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be caused by *H. longicornis*, the SFTS virus was identified not only in *H. longicornis* but also in *Amblyomma* and *Ixodes*.^{17,20} Tick bite sites are highly important clinical clues to the diagnosis of tick-borne infectious diseases.

Although chigger-related eschars can be found anywhere on the human body,^{11,12} chiggers reportedly prefer folded and damp skin areas such as in the underpants and axillary regions.^{21,22} However, few studies have investigated the preferred bite sites of mites (eschars) or ticks,³ and to the best of our knowledge, a comparative study of mite bite and tick bite sites has not been conducted.

The present study aimed to comparatively analyze mite bite and tick bite sites in humans in South Korea by investigating eschar locations in patients with scrub typhus and tick bite sites from a field epidemiological investigation.

MATERIALS AND METHODS

For mite bites, patients ≥ 18 years old, with an acute fever caused by scrub typhus, and visited Chosun University Hospital (Gwangju), St. Vincent's Hospital (Suwon), Yeungnam University Hospital (Daegu), or Eulji University Hospital (Daejeon) in South Korea between September 2004 and December 2008 were eligible for the study. When a patient with suspected scrub typhus visits any of these hospitals, they undergo a complete physical examination. Once eschars are found, the eschar locations are marked on a diagram in a prospective epidemiologic report and then recorded in the medical records. We collected and stored blood from patients and used buffy coats of the patient blood samples for PCR assay. Patients were confirmed with scrub typhus by 56-kDa gene targeting nested PCR and indirect immunofluorescence assay (IFA).

For tick bites, patients were selected based on a survey of tick contact conducted from July 2014 to December 2014 during a field study in Chonnam Province, South Korea. In that questionnaire, we asked the survey recipients to draw the tick bite site by their own on a human figure diagram as shown in Figure 1. We did not identify tick or mite species in this study.

This study was conducted with the approval of the Institutional Review Board (IRB) of Chosun University Hospital (IRB 2014-04-007). Informed consent was obtained from all participants.

Patients with ≥ 2 eschars or bite sites were excluded. Mite and tick bite sites on the human body were divided into head and neck, anterior chest including the axillary regions, back, abdominal regions including the inguinal areas, upper extremities, and lower extremities and were marked on diagrams and compared.

Standard *O. tsutsugamushi* (Boryong, Karp, Kato, Gilliam) antigens were used in an IFA test to detect immunoglobulin (Ig) M and IgG antibodies in patient sera using a modification of the method described by Robinson and others.²³ Serum samples were considered scrub typhus positive on the basis of either a single IFA IgM titer of $\geq 1:10$ against *O. tsutsugamushi* or a 4-fold or greater increase in the IFA IgG titer in the acute and convalescent stages.²⁴

Genomic DNA was extracted from buffy coats of leukocytes using a QIAamp DNA Mini Kit (Qiagen, Hilden, Germany). Nucleotide primers targeting the gene encoding the Gilliam type 56-kDa antigen in *O. tsutsugamushi* were

used, and nested PCR was performed as described by Lee and others²⁵ and Kim and others.²⁴

Red dots for mite and tick bite sites were marked on each diagram (Figure 1), and differences in mite and tick bite sites and differences by host gender were analyzed using Pearson's χ^2 tests. Statistical significance was set at < 0.05 , and data were analyzed using SPSS 18.0 for Windows (SPSS Korea, Seoul, Korea).

RESULTS

Of the 780 eligible patients with mite bites, 605 patients were included based on the medical records. Of the 510 patients with confirmed scrub typhus by PCR and IFA, four patients with ≥ 2 eschars were excluded, resulting in 506 patients with mite bites in the final sample.

Of the 111 patients who reported experiencing tick bites during the previous year in the field survey, 20 patients with ≥ 2 bite sites were excluded, resulting in 91 patients with tick bites in the final sample.

Mite bite sites were most frequently observed on the anterior chest, including the axillary region (147 patients, 29.1%), and tick bite sites were most frequently observed on the lower extremities (30 patients, 33.0%) (Table 1). There was a statistically significant difference between mite and tick bite sites ($P < 0.001$).

The highest frequency of mite bites in men ($N = 188$) was on the abdominal region, including the inguinal area (53, 28.2%), and the highest frequency of mite bite sites in women ($N = 318$) was on the anterior chest, including the axillary region (109, 34.3%) (Table 2). The difference in the distribution of the mite bite sites between genders was statistically significant ($P = 0.001$).

The highest frequency of tick bites was on the lower extremities for both genders (nine male patients, 34.6%; 21 female patients, 32.3%; $P = 0.985$) (Table 2).

The difference between mite bite and tick bite sites was not significant in men ($P = 0.234$), but was significant in women ($P < 0.001$).

Overall, eschars corresponding to mite bite sites were usually observed in joint regions where the skin is folded (Figure 1), specifically in the axillary region, inguinal area, and popliteal fossa. In addition, they were frequently observed in the external genitalia regions, including the umbilical region. Although eschars were frequently observed in the breast regions and on the back in women, they were rarely found on the breasts or backs of men. On the lower extremities, eschars were mostly found in the knee areas, specifically in the popliteal fossa rather than on the anterior knees.

DISCUSSION

Ticks tend to prefer specific hosts such as humans and wild and domestic animals depending on the species and lifecycle stage. The factors affecting the spread of tick-borne infectious diseases include the tick species and lifecycle stage, duration of adherence to the host, site of adherence, location of human activity, and geographical and weather conditions.^{17,26} Scrub typhus can be diagnosed using an antibody test or PCR, and treatment usually begins based on the identification of eschars, even before antibody test results are available for most patients. Therefore, early detection is critical for

FIGURE 1. (A) Body surface division of six site regions, and comparison between (B) mite bite sites and (C) tick bite sites, by gender. (Male front, male back, female front, and female back in order.)

timely treatment.²³ Eschars, which correspond to the bite sites by *Trombiculid* species, are one of the most critical findings for diagnosis. The reported differences in the rate of eschar detection are substantial depending on investigators and vary from 19% to 94% among scrub typhus patients.^{27,28}

In Korea, most studies have reported that scrub typhus is more frequently found in women than in men,⁷ and the

present study also identified a higher prevalence in women. This difference was associated with a higher proportion of rural women and was also affected by work characteristics. Because men worked with tools while standing in rice paddies, whereas women worked with their bare hands while squatting in the fields, women had a greater exposure to acaridans than men.²⁹

TABLE 1
Comparison of mite bite and tick bite sites

Site	Mite bite n (%)	Tick bite n (%)
Head, face, and neck	31 (6.1)	3 (3.3)
Front chest above umbilicus (including the axilla)	147 (29.1)	7 (7.7)
Back	48 (9.5)	3 (3.3)
Front and rear areas within 30 cm below the umbilicus (including the perineal, inguinal, and buttock areas)	132 (26.1)	24 (26.4)
Upper extremities	56 (11.1)	24 (26.4)
Lower extremities	92 (18.2)	30 (33.0)
Total	506 (100)	91 (100)

Student's *t* tests were performed to compare the mite bite and tick bite sites at each body sites. There was a statistically significant difference between mite and tick bite sites ($P < 0.001$).

In this study, mite bite sites were usually located at damp areas of the body, whereas tick bite sites were not limited to specific areas, findings consistent with the results reported by Chae and others.³⁰

In the present study, eschars were most frequently observed where the skin was folded around joints, particularly in the axillary region, inguinal area, and popliteal fossa, as well as in regions hidden by underpants, such as the inguinal area and external genitalia, including the proximal umbilical region. Regarding the knee area, eschars were observed more often at the popliteal fossa than at the anterior knee, especially at the sides of the popliteal fossa where the skin begins to fold rather than in the middle of the popliteal fossa, where the skin is completely folded when squatting. Similarly, Kim and others²² reported that eschars from mite bites are frequently found in regions of folded and damp skin such as inside the underpants, the axillary region, and the popliteal fossa; eschars were most frequently found within a 30-cm area below the umbilicus in men and women and the anterior chest, including the axillary area over the umbilicus, in women. In the present study, women had eschars around the breasts and on the back, whereas men rarely had eschars in these areas. Chiggers are unable to fly; instead, they climb the human body from regions closest to the ground, such as the feet, ankles, and calves, and bite where their movements are hampered (e.g., tight clothes, folded skin, contact with clothes, or areas of high pressure because of a belt or a brassiere that results in warm and damp skin).^{31,32} Therefore, the observed gender-based difference might be due to the damp areas caused by brassiere straps on the back in women and the need to squat to urinate in the

bushes; mites might access the neck in contact with tall grass, resulting in bites on the back in women. As such, these characteristic differences in eschar formation by gender seem to be due to pressure and moisture caused by brassieres, tight underwear, and knee bending.

Ticks have different preferences for host type and body region depending on the life cycle stage. For example, larvae and nymph instars reportedly prefer small animals over large animals and immature 0- to 9-year-old children over adults. Also, instars tend to prefer thinner skin such as that of the axillary regions, eyelids, popliteal fossa, and ears.^{17,26,33} The most common site of attachment varies between individual species, with *Ixodes* preferring the trunk, *Amblyomma* preferring the lower extremities, and *Dermacentor* preferring the head, neck, or upper trunk.³⁴ In another study, adults of *Haemaphysalis* spp., *Dermacentor* spp., and *Rhipicephalus* spp. preferred young adults, and in particular, *Dermacentor* spp. preferred hairy areas in animals five times more than other areas, demonstrating the differences in preferred areas depending on species.¹⁷

In addition, more mite bite sites were on the upper body including the anterior chest and axillary region, whereas more tick bite sites were observed on the lower extremities in the present study (Table 1). Chiggers prefer thinner skin, including that of the axillary region, eyelids, popliteal fossa, and ears, whereas ticks in the adult stage prefer the extremities; most ticks that bite humans are in the nymph or adult stage.

The present study presented accurate data by analyzing eschars, which are mite bite sites, on patients who had confirmed scrub typhus using IFA and nested PCR on the 56-kDa gene. However, the study was limited by the retrospective nature of the tick bite data, which was collected via a field study using a questionnaire. Survey recipients marked sites of tick bites that they had received within the past year on diagrams based on recall; therefore, the accuracy of the information could not be assessed. In addition, the tick species could not be confirmed. Further systematic studies should be conducted to accurately determine bite site preferences for ticks and mites according to species.

In conclusion, this is the first study showing that eschars, which are mite bite sites, were most frequently identified on the anterior chest, including the axillary region, and abdominal region, including the inguinal area, whereas most tick bite sites were observed on the lower extremities. Furthermore, the most frequent mite bite sites in men were the abdominal region, including the inguinal area, and lower extremities, whereas in women they were most frequently observed on

TABLE 2
Comparison of mite bite sites and tick bite sites by gender

Bite sites	Mite bite (N = 506) n (%)		Tick bite (N = 91) n (%)	
	Men (N = 188)	Women (N = 318)	Men (N = 26)	Women (N = 65)
Head, face, and neck	9 (4.8)	22 (6.9)	0 (0)	3 (4.6)
Front chest above umbilicus (including the axilla)	38 (20.2)	109 (34.3)	2 (7.7)	5 (7.7)
Back	15 (8.0)	33 (10.4)	1 (3.8)	2 (3.1)
Front and rear areas within 30 cm below the umbilicus (including the perineal, inguinal, and buttock areas)	53 (28.2)	79 (24.8)	7 (26.9)	17 (26.2)
Upper extremities	28 (14.9)	28 (8.8)	7 (26.9)	17 (26.2)
Lower extremities	45 (23.9)	47 (14.8)	9 (34.6)	21 (32.3)
<i>P</i> value	0.001*		0.985	

*Student's *t* tests were performed to compare the mite bite and tick bite sites by gender.

the chest, including the axillary region, and abdominal region, including the inguinal area, showing a significant difference by gender. However, tick bite sites were not different between men and women. The present study should help establish a rapid diagnosis of mite- or tick-borne infections through improved recognition of mite and tick prone areas by physicians and reduce complications caused by a delay in diagnosis.

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