Original Article

Epidemiological survey of tick bites occurring in Hyogo Prefecture from 2014 through 2018

Yukako Inoue, Masaru Natsuaki* and Kiyofumi Yamamishi

*Corresponding author: natsuaki@hyo-med.ac.jp
Department of Dermatology, Hyogo College of Medicine, 1–1 Mukogawa-cho, Nishinomiya, Hyogo 663–8501, Japan

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Abstract: The present report summarizes 519 cases of tick bites in Hyogo Prefecture over 5 years from 2014 through 2018. There were 222 male and 297 female cases, and ages ranged from 0 to 95 years old. The most common age group was the 70 to 79 age range (n=124). Tick bites were especially frequent in May, June, and July. The causative ticks in 431 tick bite cases were identified as Amblyomma testudinarium (AT), followed by 72 cases involving Haemaphysalis longicornis ticks, and 7 cases involving Haemaphysalis hystricis ticks. Among the 431 AT bites, 61 cases developed erythema larger than 50 mm in diameter at the bite site, and those patients were diagnosed with tick-associated rash illness (TARI). Although tick-borne diseases such as severe fever with thrombocytopenia syndrome (SFTS) and Japanese spotted fever (JSF) that are related to the above-mentioned tick species were reported in Hyogo Prefecture, there were no patients who presented with such diseases in the current report. Our findings suggest that SFTS or JSF infections that develop after tick bites are most likely accidental occurrences and that dermatologists in western Japan should pay attention to TARI as a differential diagnosis of Lyme disease in tick bite cases.

Key words: Amblyomma testudinarium, Haemaphysalis longicornis, Hyogo Prefecture, tick bite, tick-associated rash illness

INTRODUCTION

Ticks belong to the order Acarina and can be divided into the family Ixodidae and the family Argasidae. There are over 46 known tick species in Japan (Takada et al., 2019a). Ticks primarily live in either mountainous regions or grasslands including river basins and suck blood from mammals and birds. In areas with large tick populations, people are often bitten by ticks during agricultural work and outdoor leisure. Patients with tick bites often remove the tick themselves and do not visit a medical clinic.

In 2013, cases of severe fever with thrombocytopenia syndrome (SFTS), which is a tick-borne viral infection, were reported in Japan. SFTS has a high mortality rate that has attracted much public attention. As a result, the Japanese people are now more concerned with tick bites and are more frequently visiting clinics after tick bites for treatment.

Hyogo Prefecture is located in the midwestern part of Honshu, Japan. This prefecture is defined by regions of diverse environmental characteristics, including the large metropolitan area of Kobe City, expansive farming areas with fields and mountains, and islands off the seacoast. There have been reports of patients with tick-borne diseases such as SFTS and Japanese spotted fever (JSF) in this area of Japan. Accordingly, the high mortality rates associated with SFTS have attracted significant public attention and concerns, and it is essential to understand the epidemiology of tick bites. The present report investigates tick bite cases that occurred in Hyogo Prefecture from 2014 through 2018.

METHODS

1. Cases

In this study, 519 cases of tick bite patients were investigated from among those who visited medical clinics in Hyogo Prefecture in the 5 years from 2014 through 2018. Medical information was provided by medical institutions, including those belonging to the Hyogo Dermatologists Association. This study was reviewed and approved by The Ethics Review Board of Hyogo College of Medicine (No. 1416, No. 2268).

2. Study parameters

The following parameters were reported for each patient: age, sex, the causative tick species, tick blood-feeding condition, incidence of tick bites, tick bite site on the body, skin symptoms at the tick bite site (i.e., erythema), tick removal method, antibiotic use, and geographic location where the tick bite occurred.
RESULTS

1. **Age and sex of tick bite patients**
   Fig. 1 shows the age and sex of tick bite patients. There were 519 patients in total (222 males and 297 females) with ages that ranged from 0 to 95 years old. Among them, 124 patients (23.9%, 47 males and 77 females) were in their seventies, which was the most common age group.

2. **Number of tick bite cases per month**
   The number of tick bite cases reported each month in Hyogo Prefecture is summarized in Fig. 2. Tick bites occurred from March through December but were most common in June (129 patients), followed by May (116 patients) and July (108 patients). Overall, there were 353 tick bite patients identified from May through July, accounting for 68% of all patients. Nymph-stage *Amblyomma testudinarium* Koch (AT) tick bites were most prevalent in June (101 patients, 23.4% of all AT bites), and tick bites from adult-stage *Haemaphysalis longicornis* Neumann (HL) were most prevalent in August (20 patients, 27.8% of all HL bites) (Table 1).

3. **Causative ticks, blood-feeding conditions, and bite sites**
   The causative tick species are listed in Table 2. AT was the most common causative tick species and was identified in 431 cases caused by ticks in the following life stages: 31 adults, 389 nymphs, and 11 larvae. The second most common species was HL, with 72 tick bites by 40 adults, 27 nymphs, and 5 larvae. These two species are the predominant causative ticks in Hyogo Prefecture. Other species were also identified: *Haemaphysalis hystricis* Supino (HH), *Ixodes ovatus* Neumann (IO), *Haemaphysalis flava* Neumann (HF), *Ixodes monospinosis* Saito (IM), *Ixodes nipponensis* Kitaoka et Saito (IN), and *Dermacentor taiwanensis* Sugimoto (DT).

We divided the blood-feeding conditions of these ticks into three groups: not feeding (non-engorged body), insufficient feeding (slight to moderately engorged body), and sufficient feeding (completely engorged body). Fig. 3 shows representative images of the three blood-feeding conditions for AT nymphs. The percentage of ticks in each blood-feeding condition was 21% in the not feeding group, 54% in the insufficient feeding group, and 25% in the sufficient condition.
Excluding 25 patients with multiple bites by larvae, the tick bite sites in the remaining 478 patients with AT and HL bites are reported in Table 3. There were 38 head and neck bites (18 AT, 20 HL), 40 upper limb bites (35 AT, 5 HL), 188 trunk bites (173 AT, 15 HL), and 212 lower limb bites (186 AT, 26 HL). There were 66 patients with abdominal bites, which was the most frequently bite area of the trunk (62 AT, 4 HL). The lower body below the abdomen and lumbar region accounted for 327 bite sites (297 AT, 30 HL), which was 68.4% of all bite sites. Many bites were identified on covered areas such as the abdomen, back, and thighs. Only 18 (4.4%) AT bites were located on the head and neck versus 20 (30%) HL bites. Thus, the predominant area for AT bites was the lower body, whereas the head and neck regions were the predominant area for HL bites.

4. **Erythema at the site of AT bite cases**

The size of erythema that developed at the bite site by AT are shown in Fig. 4. There were 205 patients who did not develop erythema, while 165 patients developed erythema smaller than 50 mm in diameter. In 61 patients (14%), erythema larger than 50 mm in diameter formed at the bite site. Erythema did not form in patients with tick bites caused by other tick species. The representative clinical presentation of AT bites with no erythema (Fig. 5A and 5B), small erythema (Fig. 5C), and large erythema (Fig. 5D) are shown. Common symptoms such as fever, fatigue, and arthralgia were not observed in the AT bite patients with no erythema nor in those patients with large
erythema.

5. Tick removal methods and use of antibiotics

The method for removing ticks embedded in the skin is shown in Table 4. A total of 154 patients (29.7%) visited a clinic and had the tick removed with surrounding skin under local anesthesia, which was the most common tick removal method. This was followed by 123 patients (23.7%) who removed the tick themselves. Other methods included using forceps to remove the tick, applying petrolatum to the tick, and using a tick removal device. The tick removal device was used for 12 cases from 2014 to 2016, 19 cases in 2017, and 35 cases in 2018. This indicates that an increasing number of doctors used a tick removal device because of its usefulness. There were also some cases where the tick became engorged and dropped off spontaneously.

Regarding the use of antibiotics, 178 patients (34%) received antibiotics, including 123 patients (69%) who received tetracyclines.

6. Geographic location where tick bites occurred

Fig. 6 shows the location of Hyogo Prefecture. The Seto Inland Sea defines the southern border, and the Sea of Japan defines the northern border. We divided Hyogo Prefecture into 5 areas of Hanshin, Tamba, Tajima, Harima, and Awaji. The Hanshin area is located in the southwestern part of Hyogo Prefecture.

| Methods for tick removal                          | Case (%) |
|--------------------------------------------------|----------|
| Skin resection under local anesthesia             | 154 (29.7) |
| Removing ticks by patients                        | 123 (23.7) |
| Using a tick removal device                       | 66 (12.7)  |
| Using a forceps                                   | 57 (11.0)  |
| Applying petrolatum to the tick                   | 46 (8.9)   |
| Spontaneously dropping off                         | 41 (7.9)   |
| Others                                            | 32 (6.2)   |
| **Total**                                         | **519 (100.)** |

Fig. 4. Erythema at the bite site by *Amblyomma testudinarium*.

![Fig. 4](image)

Fig. 5. Clinical presentations of bite sites by *Amblyomma testudinarium*.
A: No erythema at the bite site by a nymph. B: No erythema at the bite site by an adult male. C: Erythema about 15 mm in diameter at the bite site by a nymph. D: Erythema larger than 50 mm in diameter at the bite site by a nymph.
and includes several large cities like Kobe City, Ashiya City, and Nishinomiya City. Additionally, the Rokko Mountain Range are in this area. The Tamba area is located in the mid-eastern part and consists mostly of mountains and forests. The Tajima area is in the northern part and is also mostly mountainous. The Harima area is in the southern part and contains many fields and low mountains. Awaji is an island mostly covered by mountains and forests in the eastern part of the Seto Inland Sea.

Fig. 7 shows the geographic locations where tick bites occurred. There were 154 patients who were bitten by 6 tick species in the Hanshin area, including 3 cases of HH nymphs, followed by 133 patients in the Awaji area that included also 10 cases of AT larvae, 4 cases of HH (3 adult female and 1 nymph). There were 132 tick bites in the Harima area, 85 tick bites in the Tajima area, and 15 tick bites in the Tamba area. Based on our calculations, AT nymph bites were more common than bites from AT adults (approximately 15–25 times) in the Tajima, Awaji, and Hanshin areas including the Rokko Mountains. This suggests that there is a high population of AT ticks in rural and natural areas.

Discussion

There have been many reports about tick bite cases in Japan (Hasegawa et al., 2016; Noda et al., 2018; Tominaga et al., 2013). Yamaguchi (1994) summarized 796 cases and reported that *Ixodes persulcatus* Schulze (IP) and IO were prevalent in Japan from the Kanto and Chubu to other northern regions, while AT and HL were common from the Kinki to southern regions. In the current study, most of the tick bites that occurred in Hyogo Prefecture were by AT nymphs. AT is found from the Kanto to more southern regions, and the distribution has expanded north to Hokuriku and Tohoku regions recently (Takada et al., 2019a). Adult AT are 6–8 mm in length, while nymphs are only about 2 mm in size. Wild boar and bear frequently act as the host for AT, which mainly live in the brush forests of mountainous areas and the surrounding grasslands in Hyogo Prefecture. AT is the species most likely to bite humans in the western part of Japan (Okino et al., 2007a).

On the other hand, 72 patients were bitten by HL and many of those were by adult ticks. HL is widely prevalent in Honshu, Shikoku, Kyushu and also northern Japan (Takada et al., 2019a). Adult HL are about 3 mm in length. Grazing cattle often act as the host for this species, but HL is also present in grassland areas near homes, as well as in the mountains (Okino et al., 2007b).

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AT: *Amblyomma testudinarium*, HL: *Haemaphysalis longicornis*, HH: *H. hystricis*, IO: *Ixodes ovatus*, HF: *H. flava*, IM: *I. monospinosus*, IN: *I. nipponensis*, DT: *Dermacentor taiwanensis* (M: adult male, F: adult female, N: nymph, L: larva).
In the present study of tick bites in Hyogo Prefecture, there were 222 male patients and 297 female patients, seeming that ticks had a preference for females. The patients ranged in age from 0 to 95 years old. Patients in their seventies comprised the largest age group, and 274 patients were in their sixties or older, accounting for 53%. These findings were considered to reflect the fact that people in this age range have more opportunities for outdoor leisure and farm work. The tick bite season was mainly May through July, which is consistent with the active period for ticks. However, AT bites showed a peak in May to June, while HL bites peaked in August. This was because AT bites were often caused by nymphs, which has the predominate life stage during May to June, and HL bites were generally from adult ticks, which has the predominate life stage in August.

Bites on the lower body accounted for about 68% of the total bites in the current study. Okino et al. also reported that AT bites occur more frequently on the lower body (Okino et al., 2007a). Additionally, only 4.4% of AT bites were located on the head and neck versus about 30% of HL bites, showing differences in common bite sites between species. Interestingly, areas covered by clothing were preferentially bitten by both species. Among the 38 patients with head and neck bites, 19 patients were children aged 0–15 years old. This suggests that children are more susceptible to being bitten on the head or neck.

In Japan, tick-borne diseases include rickettsial infections such as JSF, viral infections such as SFTS, and borreliosis such as Lyme disease (Takada, 2011; Yamaji, 2018). JSF mainly occurs west of the Kanto region. In Hyogo Prefecture, several JSF cases have been reported annually, with 16 cases in the Rokko Mountain Range from 2014 to 2018 (Kanzaki et al., 2018; Takada et al., 2019b). Patients with SFTS have been identified west of the Kinki/Hokuriku regions since 2013 (Fukushi and Saijo, 2013; Kishimoto and Kida, 2013; Morikawa, 2015). In Hyogo Prefecture, 2 cases of SFTS occurred in the Tajima area (Takada et al., 2019a). The fact that the fatality rate of SFTS is approximately 20% (Saijo, 2018) terrifies tick bite patients.

AT and HL are both competent vectors of SFTS, and HH and DT are both considered to be vectors of JSF; although DT as a causative tick is rare in humans (Takada et al., 2019a). However, there were no known patients who developed JSF or SFTS after being bitten by ticks in this study. Yamauchi et al. (2010) investigated the presence of pathogenic DNA in AT by PCR analysis using samples obtained from Hyogo, Okayama, and Hiroshima Prefectures. They reported that genera *Borrelia*, *Rickettsia*, and *Anaplasma* were not detected. AT may be a carrier for *Rickettsia tamurae*, but only one case with unknown pathogenesis has been reported in Japan (Imaoka et al., 2011). According to the studies conducted so far, viral or rickettsial infections that develop after tick bites are likely accidental occurrences in Hyogo Prefecture.

Expanding erythema migrans (EM) is a characteristic finding in patients with Lyme disease that develops after being bitten by IP. EM associated with Lyme disease is at least 50 mm in diameter but can be much larger (Stanek et al., 2012). IP infected by the *Borrelia* species causing Lyme disease are only found in Hokkaido and the mountains of central Honshu in Japan, and it is generally considered that Lyme disease does not occur after tick bite in other regions (Hashimoto et al., 2002). On the other hand, 61 of the 519 patients in this study developed erythema larger than 50 mm in diameter after being bitten by AT. Natsuaki et al. (2013) proposed that if Lyme disease could not be confirmed in patients with EM following a tick bite, they should be diagnosed as having tick-associated rash illness (TARI). The 61 patients in our study appear to have had TARI. Although its pathogenesis is unknown, it is considered that TARI represents a delayed-type allergic reaction to substances in tick saliva (Natsuaki et al., 2014). Our preliminary data shows that of the 61 patients with TARI, 34 cases (56%) had a history of prior tick bites, while only 18 (8.8%) of the 205 patients with no erythema had a history of prior tick bites. Although obtaining a history of tick bites is dependent on the patient’s memory, this finding suggests that an allergic reaction to tick-derived substances is involved in the pathogenesis of TARI.

Recently, some reports showed that tick bites by HL or AT might be a possible cause of red meat allergies in Japan (Chinuki et al., 2016; Hashizume et al., 2018; Chinuki and Morita, 2019; Hashizume, 2019). However, there were no documented clinical cases of beef allergies in the medical history of tick bite patients in this study (data not shown). This indicates that the probability of becoming sensitive to red meat allergens after tick bites is very low, but dermatologists should pay close attention to any allergic reactions that may develop after tick bites.

The most common and most reliable tick removal method was en bloc resection of the tick and surrounding skin under local anesthesia at a medical clinic. However, many patients removed the tick themselves. In such cases, the mouthparts may remain in the skin, and complete removal may not be achieved. Therefore, it is necessary to educate the general public that it is recommended to visit a clinic for tick removal after a tick bite (Natsuaki, 2017). The use of antibiotics by each tick bite patient was also investigated. We found that 69% of all prescribed antibiotics were tetracyclines, possibly as a precaution against the development of tick-borne infections. However, antibiotics are not effective against the viral infections such as SFTS. JSF and Lyme disease only
occur in specific regions of Japan and there are any side effects with antibiotic therapies. Accordingly, it is recommended that prophylactic antibiotics should not be given indiscriminately for the prevention of tick-borne infections (Natsuaki, 2017).

In conclusion, the risk of developing JSF or SFTS after a tick bite in Hyogo Prefecture is low and the onset of these diseases after tick bites is most likely an accidental occurrence. However, we cannot completely rule out the possibility. Therefore, ticks should be removed immediately by a doctor. It is also crucial to pay close attention to fever, skin rash, or digestive symptoms that may develop during the subsequent 1 to 2 weeks after a tick bite. The patients and dermatologists should also be monitored for the development of TARI after AT bites, because it may lead to the differential diagnosis of Lyme disease. Thus, dermatologists, medical clinics, and the general public, especially those in the western part of Japan, should be fully aware of these points so that tick bite patients receive proper treatment.

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Conflict of Interest

The authors have no conflict of interest.

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