

Original article:

Tick-borne relapsing fever in Sabzevar (Khorasan Razavy Province), North-Eastern Iran

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Abstract

Background: Soft ticks play an important role in transmission of bacteria, rickettsia and viral diseases to human. In Iran soft ticks of the genus *Ornithodoros* spread the tick-borne diseases. **Objective:** Present study was performed to investigate the latest situation of tick-borne relapsing fever (TBRF) among people and tick infectivity to *Borrelia* in Sabzevar, an endemic tick-borne relapsing fever region in Iran. **Methodology:** Ticks were collected in the sampled areas of Sabzevar County by clustered random sampling. The suspected cases of TBRF were passively detected in the study villages. Each of *Ornithodoros tholozani* was separately crushed and resultant homogenate was inoculated intraperitoneally into a white mouse. **Results:** A total of 3892 soft ticks were collected and identified. The *Argas* and *Ornithodoros* genus were observed 69.6 % and 30.4 %, respectively. *Argas persicus*, *Ornithodoros lahorensis*, *O. tholozani* and *A. reflexus* species were found 68.0 %, 25.6 %, 4.8% and 1.6 %, respectively. *A. persicus* (68.0 %) and *A. reflexus* were found as the highest and the lowest frequent species. Totally 5.2 % of *O. tholozani* ticks infected with *Borrelia persica*. Among individuals who suspected to the TBRF, 5 cases infected with *B. persica*. **Conclusions:** The vector infectivity rates were 5.2 % which can be an important factor and ability to make proper decision for better TBRF management and revision of control measures. Also this study raises our country TBRF epidemiological aspects and improves them.

Keywords: *Borrelia persica*; *Ornithodoros tholozani*; TBRF; Tick-borne relapsing fever

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Introduction

Ticks transmit the widest variety of pathogens of any arthropod blood sucking agents, including bacteria, rickettsia, protozoa, and viruses¹. Tick-borne relapsing fever (TBRF) is a zoonotic disease transmitted worldwide by soft ticks of the genus *Ornithodoros*. It transmits at least 15 distinct *Borrelia* species throughout the world². The disease is reported from North and South America^{3,4}, Africa⁵⁻⁷, Asia⁸ and Europe⁹. *Ornithodoros* is widely distributed throughout

India and Kashmir, the southern countries of the former USSR (Kazakhstan, Kyrgyzia, Tajikistan, Turkmenistan, and Uzbekistan), Iran, Iraq, Syria, Jordan, Turkey, Occupied Palestine, Egypt, and Cyprus. Relapsing fever possibility exists in Afghanistan, Pakistan, and Libya^{8,10,11}. The epidemiology of the disease depends on the relationships between the tick and *Borrelia* species as well as environmental condition in the distribution areas in each region. Reservoir hosts are usually wild rodents².

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In Iran, TBRF is an acute febrile and one of the endemic diseases which mainly caused by *Borrelia persica* and transmitted by *Ornithodoros tholozani* species. Retrospectively, *Ornithodoros tholozani* and *Borrelia persica* were first identified and reported from Iran¹². *O. tholozani* distribution areas overlap with clinical relapsing fever cases whose cause by *B. persica*. *B. persica* has a wide geographic distribution and is present mainly in east and west Azarbaijan, Ardabil provinces and in Alborz and Zagros mountain chains^{13,14}. TBRF is also endemic in the north-west of Iran where clinical and epidemiological studies have been conducted^{15,16}. Ardabil province is the first ranked infected area, followed by Hamadan, Zanjan, Kurdistan and Qazvin provinces sequentially¹².

Tick-borne relapsing fever is still a health problem in the rural areas. Since understanding its vector infectivity is an important factor in any tick-borne relapsing fever epidemiological study, and to make proper decision for management and revision of the control measures. Thus current study was performed to investigate the latest situation of tick-borne relapsing fever and tick infectivity rates to *Borrelia* in Sabzevar endemic region, Khorasan Razavi province in North-Eastern Iran.

Material and Methods

Study Area

Khorasan Razavi province is the newest provinces of Iran which has been established from dividing of Khorasan province, located on the north-eastern

frontier of Iran (Fig. 1). The center of this province is Mashhad which located at an altitude of about 970 m above the sea level, 36° 17' N, 59° 36' E. It is limited from north to North Khorasan province and Turkmenistan, from east to Afghanistan, from south to South Khorasan province, from west to Semnan province and from South western to Yazd (Fig. 1). From view of natural location, it divided into two parts, northern and southern. The northern part is mountainous region with valleys and low regions which have fertile plains. The southern part has been formatted from vast low plains with low altitude hills. From climate situation, it lies in the temperate northern region which has a various climates with an average of temperature between 13.6 and 17°C and average of rainfall about 218 mm/year.

The county 'town' of Sabzevar (55° 28' - 61° 20' N, 30° 21' - 38° 17' E; at an altitude of about 950 m above the sea level) lies in the west of this province, in the north eastern of Iran at 200 km from of the west of the Mashhad (Fig. 1), and has a population of about 214,582. Most of the people work in the agricultural and animal husbandry in close to livestock, and are being exposed to ectoparasites such as soft ticks, which infected with the pathogens. They transmit diseases to the people. For the present study, 52 villages that each held at least 20 households were randomly selected from the 260 villages that together form the county town.

The study was ethically approved by ethics committee.

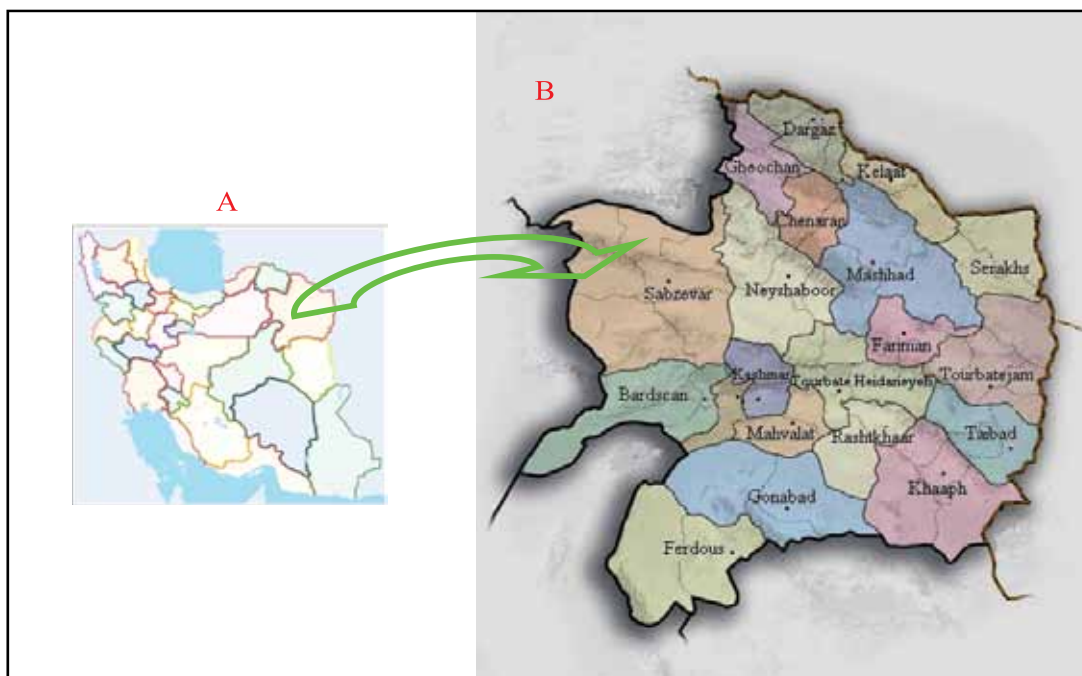


Figure 1: Location of the study area; (A) Map of Iran, (B) Map of Khorasan Razavi Province.

Tick collection

Ticks were collected, both actively and passively, by clustered random sampling in the 52 sampled villages in different areas of city (mountainous and plains). In each village, 5 human dwelling and 5 animal places in the north, the south, the east, and the west and in the center were selected. For detecting TBRF suspected cases, it was often possible to determine where each case had been exposed to tick bites by interviewing's, and these areas were searched for ticks. Ticks were collected using dig-in plastic traps baited with dry ice. According to their biology, dark cracks and crevices in the walls, ceilings and floors of human and animal dwellings, caves, barns and rodent burrows were also checked for ticks. All ticks were handled with forceps and transferred into a screw capped holding tube that contained a small piece of cotton that had been moistened with 1 % mycostatin solution (to prevent desiccation and mould growth) and kept in the tube, at 5°C, until they could be identified on the basis of their morphological features¹⁷. *O. tholozani* collected were checked for borreliae.

Blood-sample Collection and Microscopy

In 2004, the suspected cases of TBRF (each with relapsing episodes of fever, chills and headache) were passively detected in the 52 study villages. Each village had its own dispensary, where each suspected case was checked for fever, nausea, asthenia and headache. A finger prick blood sample was collected from each suspected case, using a sterile lancet and a tube containing EDTA, and used to make thick and thin smears. The smears were fixed in methanol for 5 min, stained with (5%) rapid Giemsa's stain for 20 min and then examined under oil immersion, at $\times 1000$, for borreliae. All the borreliae observed were assumed to be *B. persica*. A 'suspected case' was defined as an acutely ill individual who had a clinical history typical of TBRF, who had lived in, or travelled to, an area where the disease is endemic, and who had visited a tick-infested dwelling, had contact with rodents or other small mammals, and/or had been exposed to the blood or vomit of a confirmed case of TBRF.

Rodent Inoculation

Although, it is possible to inoculate the agent to animal by an artificial membrane apparatus^{18,19}, in this study each of *O. tholozani* (a random sample of the ticks of this species that were collected) was separately crushed. Then each resultant homogenate was inoculated intraperitoneally into a white mouse. From the fourth day post-infection, wet smears of

peripheral blood, collected from the ear of a mouse, were prepared and checked for the presence of borreliae, by dark-field microscopy.

Results

A total of 3892 soft ticks were collected and identified in the study area. Among them, 1994 individuals were adults and the others were nymphs which their organs hadn't completed, therefore they eliminated from the study. The genus frequency of *Argas* and *Ornitodoros* were 69.6% and 30.4%, respectively (Fig. 2). The species frequency of *A. persicus*, *O. lahorensis*, *O. tholozani* and *A. reflexus* were 68.0 %, 25.6 %, 4.8 % and 1.6 %, respectively (Fig. 3). The highest and lowest frequency of collected species was *A. persicus* (68 %) and *A. reflexus* (1.6 %), respectively. Among the all collected *O. tholozani*, 5.2 % infected with *B. persica*. Also among individuals who suspected to the TBRF, 5 cases infected with *B. persica* in the study area by their interviewing and finger prick blood samplings.

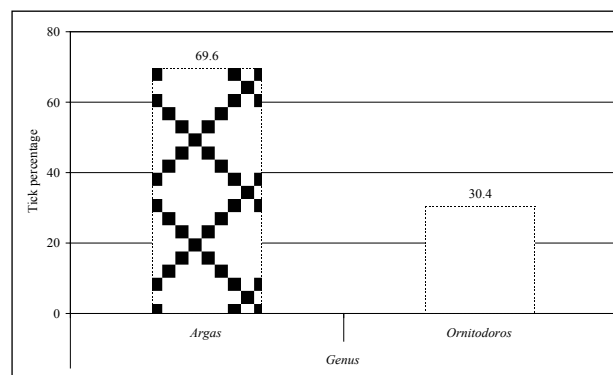


Fig. 2 Frequency of the soft ticks in the study area

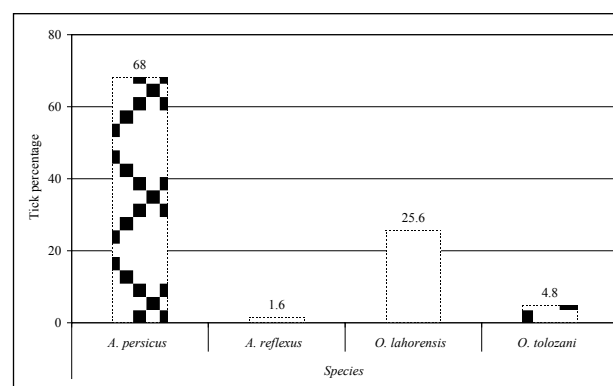


Fig. 3 Frequency of the soft tick species in the study area

Discussion

Relapsing fevers occurs in two epidemiologic forms - the louse-borne relapsing fever (LBRF) and the tick-borne relapsing fever (TBRF). TBRF is caused by a variety of different species of *Borrelia*, each

of which is transmitted by and named after, the species of *Ornithodoros* ticks that act as vectors for the organisms. Rodents and other animals serve as natural reservoirs. In contrast, LBRF is transmitted from person to person solely by human body lice which have ingested *Borrelia recurrentis*²⁰.

TBRF occurs sporadically and in small clusters throughout rural in the northern temperate region of the world. In Iran, the Crimean-Congo Hemorrhagic Fever (CCHF) and Tick-borne relapsing fever (TBRF) are the most common tick borne diseases. Tick-borne relapsing fever is an endemic disease in some parts of Iran.

In this study the *O. tholozani* which was transmitted the *B. persica* has the second ranked (25.6 %) in the collected species (Fig. 3) which can preserve the *B. persica* in the environment and transmit to human. In recent years, researchers have been reported the *O. tholozani* from the other provinces such as Semnan²¹, West Azerbaijan²², Hamadan, Qazvin, Kurdistan²³. In a study conducted by Masoumi Asl et al (2009) in the endemic areas of Iran revealed that the most prevalent ticks were *O. tholozani* and *O. erraticus* which was infected with *B. persica* and *B. microti*, respectively¹². *B. persica*, the most common cause of TBRF in Iran, has a wide geographic distribution and is present in Alborz and Zagros mountain chains¹³. In present study, among the all collected *O. tholozani* soft ticks, 5.2 % of them infected with *B. persica*. Recent similar studies from the other provinces of Iran have been showed that *O. tholozani* infected with *B. persica* including Semnan²¹, West Azerbaijan²², Hamadan , Qazvin and Kurdistan²³.

In current study human infection was found in 5 cases. The other researchers have been reported the TBRF human infection from the other regions including Ardabil, Hamadan, Zanjan, Kurdistan, Qazvin, Hormozgan, Semnan, Tehran, Khorasan, East Azerbaijan, Markazi, Mazandaran, Gilan, Qom, Golestan, Fars, Sistan and Baluchistan, and Isfahan in Iran¹². Masoumi et al (2009) reported a total of 1415 cases of the TBRF from the entire of Iran during 1997-2006¹². The highest prevalence was observed in year 2002 with the incidence rate of 0.41/100,000 population. Ardabil province is the first ranked infected area (625 out of 1415), followed by Hamadan, Zanjan, Kurdistan and Qazvin provinces sequentially¹². Mahram and Ghavami (2009) reported a case of congenital tick-borne relapsing fever with transplacental transmission¹⁵. In a recently study conducted by Moemenbellah-Fard et al (2009), 148 cases of TBRF were passively detected in Kurdistan province most (115) of them were confirmed

by microscopy²³.

In Sabzevar County, the endemic region of TBRF in Khorasan Razavi province, which present study was done not only many native people is working in agricultural and animal husbandry in close to livestock, and are being exposed to ectoparasites such as soft ticks, which infected with the pathogens but also tick-borne relapsing fever is still a health problem in the rural areas for travelers, pilgrimages and other tourists from the other provinces and immigrant from the other adjacent countries such as Afghanistan and Turkmenistan. Since, in this study the vector infectivity rates were 5.2 % which can be an important factor and ability to make proper decide decision for better TBRF management and revision of control measures. Also this study raises our country TBRF epidemiological aspects and improves them.

Because, relapsing fever is a disease characterized by relapsing (i.e. recurring) episodes of fever, often accompanied by other symptoms should be in special supervision. With seeing any initial symptoms, which usually develop within 7 days after being bitten, such as fever, generalized body aches, myalgias, arthalgias, headache, chills, sweats and other/ later symptoms such as nausea, vomiting, anorexia, dry cough, photophobia, rash, neck pain, eye pain, confusion and dizziness the person who suspected to relapsing fever should be diagnosed and treated^{24,25}.

Because, anybody of any age can develop relapsing fever, it should be suggested to prevent infection avoid sleeping in rodent infested buildings, limit tick bites by using insect repellent containing DEET (on skin or clothing) or permethrin (applied to clothing or equipment), rodent-proof buildings in areas where the disease is known to occur, identify and remove any rodent nesting material from walls, ceilings and floors, in combination with removing the rodent material, fumigate the building with preparations containing pyrethrins and permethrins. More than one treatment is often needed to effectively rid the building of the vectors, the soft-ticks. Always follow product instructions, and consider consulting a licensed pest control specialist²⁴.

Conclusion

In this study the vector infectivity rates were 5.2 % which can be an important factor and ability to make proper decide decision for better tick-borne relapsing fever management and revision of control measures. Also this study raises our country tick-borne relapsing fever epidemiological aspects and improves them.

Conflict of interest: None declared

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