

## Original Article

# Epidemiological Study of Endemic Relapsing Fever in Hamadan Province, West of Iran

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### Abstract

**Background:** Endemic relapsing fever remains under diagnosed in our area according to a low index of suspicion among clinicians, as well as its difficult diagnosis. The goal of this study was to present the epidemiological aspects of the disease in western Iran.

**Methods:** In this analytical-descriptive cross-sectional study, the epidemiological and clinical aspects of relapsing fever were investigated in Hamadan Province, western Iran from 1999 to 2013. A confirmed patient was defined as a person who had both febrile illness and detected spirochetes by Wright-Giemsa or dark-field microscopy in a peripheral blood smear. For the statistical analysis, the statistical software SPSS was used.

**Results:** During the study period, 276 cases of relapsing fever were recorded that 146 were male. Due to the age group distributions, most of the patients aged less than 20 yr. Patients noticed from April through March, most cases were reported in September (53 cases, 19.2%). Considering time trend of the mentioned disease between 1999 and 2013 showed an increasing trend of disease from 1999 to 2003 (from 2.5% to 21.0%), while the prevalence of disease had a decreasing trend after than from 21.0% in 2003.

**Conclusion:** The rate of endemic relapsing fever is similar in both male and female genders, but its prevalence reduced by increase of age. The trend of the changes in prevalence of the mentioned disease has shown to be downward in recent years probably due to improving health policies especially among children and adolescents and particularly in rural areas.

**Keywords:** Endemic relapsing fever, Tick, *Borrelia*, Epidemiology, Iran

## Introduction

Relapsing fever, is characterized by recurrent acute episodes of fever. These are followed by periods of which differ in their durations. Relapsing fever is an infection spread by the vectors of lice and ticks (Jump et al. 2004).

Tick-borne relapsing fever is mostly caused by *Borrelia* species generally called ‘Asian or Asiatic TBRF’ (Goubau 1984, Fukunaga et al. 1996, Trape et al. 2013). The geographical distribution of the *Borellia* is mostly related to Eurasia. The most important agent is *B. persica*, which causes the large majority of human cases and has the widest distribution (Dschunkowsky 1913, Baltazard et al. 1950, Colin de Verdière et al. 2011).

In Eurasia, Dschunkowsky (1913) was the first person who described the tick-borne relapsing fever (TBRF in the Ardebil region of Iran, and because of this reason it was called *Borrelia persica* (Euzeby 1997). However, in the same area, at early time in 1882, Tholozan also published the first clinical description of a case of TBRF, which he called ‘fie `vre re`currente asiatique’, and which was transmitted to humans by an *Ornithodoros* tick (Theodorides 1998). In the following decades, cases of relapsing fever were reported and described all over the Middle East region and were attributed mainly to *B. persica*, but other bacteria were also reported (Nicholson 1919, Adler et al. 1937, Kalra

and Rao 1951, Davis and Hoogstraal 1954, Babudieri 1955).

Tick-borne relapsing fever is an endemic disease in Canada (southern portion of British Columbia), Mexico, Central and South America, central Asia, Africa, the Mediterranean region, and Russia (Vial et al. 2006, Cutler et al. 2009, Platonov 2011, Diatta et al. 2012). Finally, TBRF has a mortality rate of less than 2% (in treated patients) to 4–10% (in untreated individuals) (Dworkin et al. 2002). *Borrelia duttoni* (causes TBRF), is found in East Africa and transmitted by the soft tick *O. moubata* (Carlisle 1906).

For the first time, *B. persica* was isolated and separated from the Ardabil, Northwestern Iran, from the blood smear of a patient by Dschunkowsky and Luhs in 1913. The vector of *B. persica* was first found in Iran in 1879 and after that, it was named as *O. tholozani* (Rodhain 1998, Arshi et al. 2002, Aghighi et al. 2007).

Tick-borne relapsing fever is acquired by at least 15 different *Borrelia* species (Blevins et al. 2008). In Iran, TBRF transmission to humans are mainly attributed to three species of Argasidae including, *O. tholozani*, *O. erraticus* and *O. tartokovskyi*. Furthermore, *B. persica*, *B. microti*, *B. latyschevi*, and *B. baltazardi* are the major transmitting agents of TBRF in Iran (Vatandoost et al. 2003). In Iran, principal foci of TBRF are almost mountainous provinces of north-west and west parts, and is reported from various parts situated in south and center of the country (Baltazard et al. 1948, Rodhain 1976, Aghighi et al. 2007, Rafinejad et al. 2012). People in endemic regions should aware of tick infected areas and rodents and use repellents and protective costume to impede tick bites (Dworkin et al. 2002).

This disease is almost not diagnosed in our area due to a low index of suspicion among clinicians as well as its difficult diagnosis. The aim of this study was to present the epidemiological aspects of the disease in

Hamadan Province, western Iran, during 1999–2013.

## Materials and Methods

In this analytical-descriptive cross sectional study, the epidemiological and clinical aspects of relapsing fever were investigated in Hamadan Province, western Iran (Fig. 1) from 1999 to 2013. The county's populations at the 2011 were 525794, 169352, 13711, 75445, 27645 and 20349 in Hamadan, Malayer, Razan, Nahavand, Bahar and Kabudarahang, Respectively.

Demographical, clinical, and geographical information included in the disease reporting forms and records of relapsing fever cases were requested from the health department of the Hamadan University of Medical Sciences. A confirmed patient was defined as a person who had both febrile illness and detection of spirochetes by Wright-Giemsa or dark-field microscopy in a peripheral blood smear.

Results were presented as mean±standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using Non-parametric Kruskal-Wallis H test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. Categorical variables were, on the other hand, compared using chi-square test.

For the statistical analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used. *P*-values of 0.05 or less were considered statistically significant.

## Results

During the study period, 276 cases of relapsing fever were recorded that 146

(52.9%) were male and 130 (47.1%) were female with overall mean age of  $15.89 \pm 13.69$  yr. Incidence rate was calculated 3.3/10000 population. Regarding age group distributions, most of patients aged less than 20 yr and the prevalence of the disease in patients aged less than 10 yr was 41.3%, in those aged 10 to 20 yr was 31.9%. The prevalence of disease was considerably lowered in older than 40 yr (4.7%). There has been a downward trend in the prevalence of relapsing fever by increasing age. According to the occupational status, 37.3% were rancher followed by other jobs (Table 1). There was no difference between the genders in terms of mean age, age distribution, and clinical manifestations, however occupational status was different between them ( $P < 0.01$ ) (Table 1).

Regarding clinical manifestations, most patients suffered from classic symptoms of the mentioned disease including sweating, abdominal pain, cough, fever, chilling, headache, nausea, and vomiting. Jaundice was only revealed in 8.7% and photophobia and eosinophilia were found only in 8.7% of them (Table 1). The death due to TBRF in

none of the patients in this study was reported.

Interestingly, more than half of the infected cases were found out in a city named Razan (58.3%), followed by Kabudrahang (37.3%), while the prevalence of disease in Hamadan City as the center of province was only 2.2% (Table 2).

Most cases were reported in September (53 cases, 19.2%) (Fig. 2). Almost cases were diagnosed during the summer (147 cases, 53.3%). Considering time trend of the mentioned disease between 1999 and 2013 showed an increasing trend of disease from 1999 to 2003 (from 2.5% to 21.0%), while the prevalence of the disease had a decreasing trend after than from 21.0% in 2003 to 1.1% in 2010 (Fig. 3). The trend of the changes in the prevalence of relapsing fever by gender was shown with the peak of occurrence in 2003 as 29 (19.9%) in men and in 2002 as 34 (26.2%) in women (Fig.4). In addition, assessing the age proved that the occurrence of disease within this time showed no significant changes in the trend of the age of disease occurrence (Fig. 5).

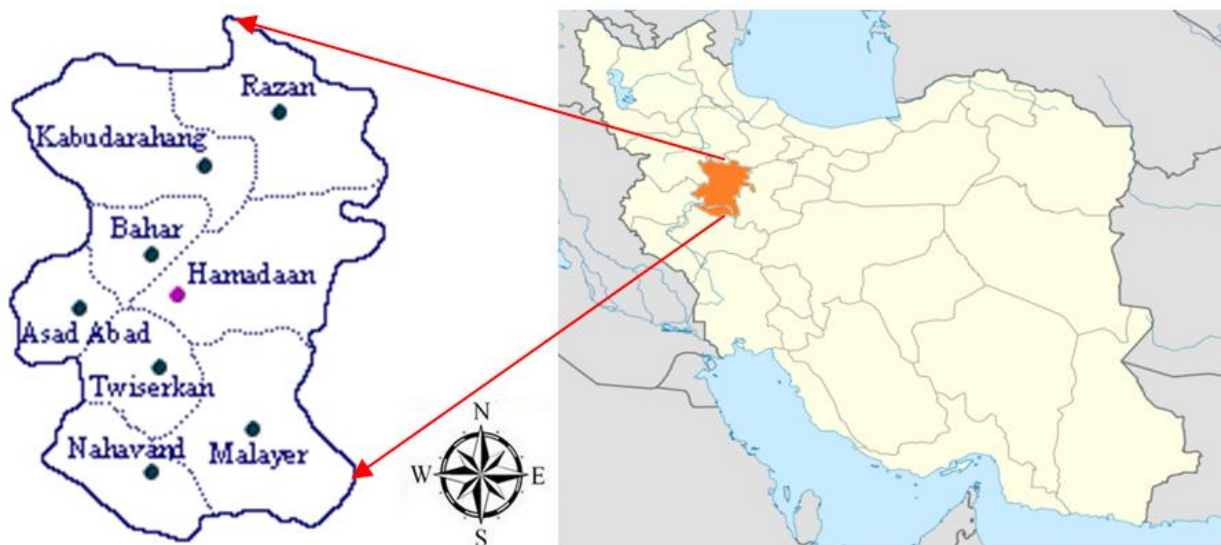


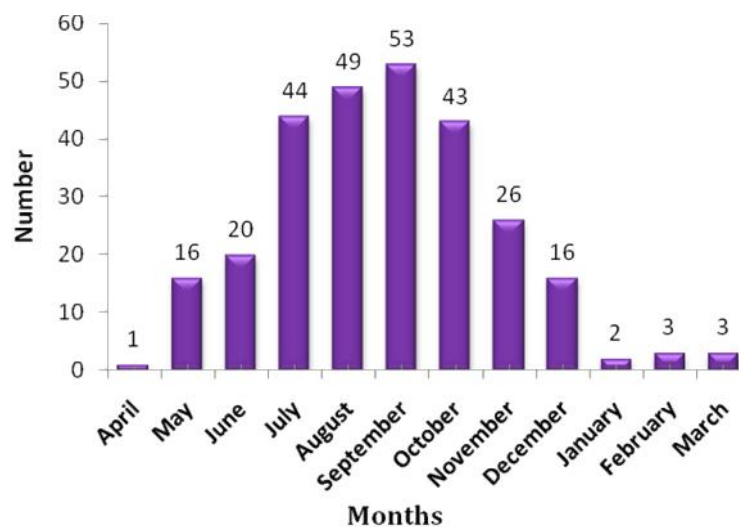
Fig. 1. Map of study area in Hamadan Province, western Iran

**Table 1.** Baseline characteristics of tick-borne relapsing fever of Hamadan Province, Western Iran (1999–2013)

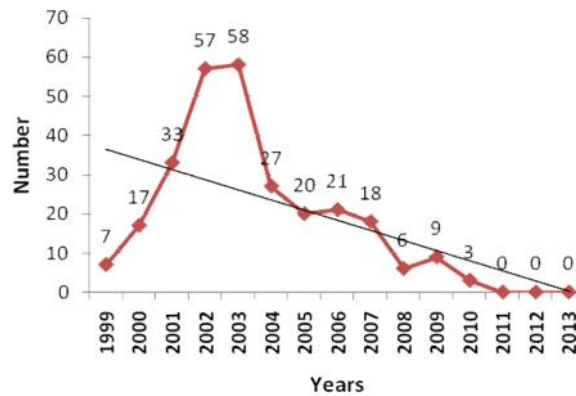
	<b>Total (n= 276)</b>	<b>Male (n= 146)</b>	<b>Female (n= 130)</b>	<b>P-value</b>
<b>Age (yr)</b>	15.89±13.69	14.55±12.50	17.40±14.82	0.088
1–10	114 (41.3)	63 (43.2)	51 (39.2)	
11–20	88 (31.9)	51 (34.9)	37 (28.5)	
21–30	35 (12.7)	13 (8.9)	22 (16.9)	
31–40	26 (9.4)	15 (10.3)	11 (8.5)	
Older than 40	13 (4.7)	4 (2.7)	9 (6.9)	
<b>Occupation</b>				< 0.001
Rancher	103 (37.3)	54 (37.0)	49 (37.7)	
Farmer	7 (2.5)	6 (4.1)	1 (0.8)	
Housekeeper	22 (8.0)	0 (0.0)	22 (16.9)	
Students	72 (26.1)	47 (32.2)	25 (19.2)	
Age under the occupation	72 (26.1)	39 (26.7)	33 (25.4)	
<b>Clinical symptoms</b>				0.128
Classic symptoms	228 (82.6)	121 (82.9)	9 (6.2)	
Classic symptoms plus Jaundice	24 (8.7)	107 (82.3)	15 (11.5)	
Classic symptoms plus Photophobia and eosinophilia	24 (8.7)	16 (11.0)	8 (6.2)	

**Table 2.** Distribution of participants of tick-borne relapsing fever according to different regions of Hamadan Province, Western Iran (1999–2013)

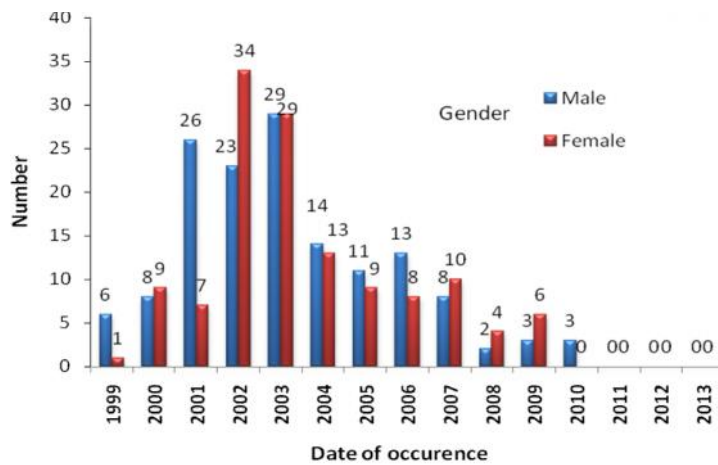
<b>Region</b>	<b>Total (n= 276)</b>	<b>Male (n= 146)</b>	<b>Female (n= 130)</b>
Hamadan	7 (2.5)	5 (3.4)	2 (1.5)
Malayer	1 (0.8)	0 (0.0)	1 (0.8)
Razan	161 (58.5)	83 (57.2)	78 (60.0)
Nahavand	3 (1.1)	1 (0.7)	2 (1.5)
Bahar	1 (0.4)	1 (0.7)	0 (0.0)
Kabudarahang	103 (37.5)	56 (38.6)	47 (36.2)



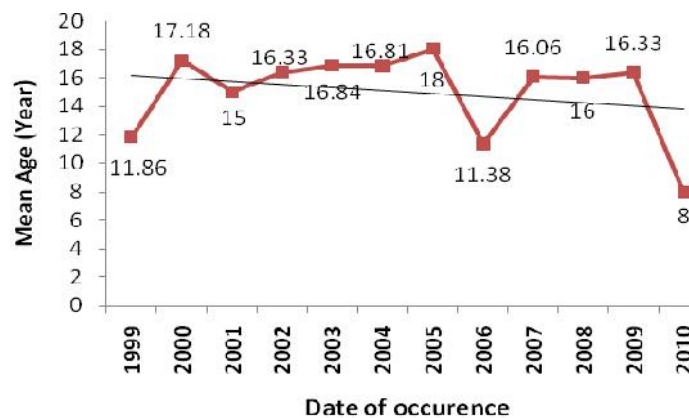
**Fig. 2.** Number of tick-borne relapsing fever cases by months in Hamadan Province, Western Iran (1999–2013)



**Fig. 3.** Number of tick-borne relapsing fever cases of different years in Hamadan Province, Western Iran (1999–2013)



**Fig. 4.** The trend of the changes in the prevalence of tick-borne relapsing fever by gender in Hamadan Province, Western Iran (1999–2013)



**Fig. 5.** The trend of the mean age of patients of tick-borne relapsing fever within study period in Hamadan Province, Western Iran (1999–2013)

## Discussion

Tick-borne relapsing fever is known as endemic disease in Hamadan Province. Our study has some important findings. A total number of 276 cases were investigated. In the study in Kurdistan Province, the TBRF cases included 50.7% women and 49.3% men (Kassiri et al. 2014) and in Ardebil Province, Iran, a total of 391 (49% females, 51% male) patients were studied from 1998–2001 (Arshi et al. 2002), which is similar to our findings. In the study of Masoumi-Asl et al. (2009), the TBRF cases included 55% women and 45% men, that results of our study is opposed. In a study in the United States from 1997 to 2000, the patients included 235 men (52%) and 178 women (40%), data regarding gender was missing for 37 (8%) (Dworkin et al. 2002), that is similar with our study.

In this study, most prevalence of the disease was 41.3%, among the age groups of 1–10 years. In a study by Croche Santander et al. (2013), the median age of patients was 11 years. Although the distribution of the disease was similar in both male and female genders ( $P > 0.05$ ), its prevalence was reduced by increase of age. Masoumi-Asl et al. (2009) reported that there were 33% of the cases younger than 5 years old, 18% of 6–10 years old and 27% of 11–20 years old. In the study of Rafinejad et al. (2012), in Kurdistan Province, Iran, 2000–2004, most frequencies of TBRF based on age groups were observed as 43.3%, 17.5% and 17.5% in 10–19, 20–29 and 0–4 years old, respectively. In a new highland endemic focus of western Iran, most (91%) of the patients were reported to be young people (Moemenbellah-Fard et al. 2009).

In this study, the rate of infection in rancher, farmer, housekeeper, students and age under the occupation was similar to the finding of Rafinejad et al. (2012) on TBRF in Kurdistan Province, western Iran. This information represented that all job groups are

at risk of obtaining infection but the majority of cases in our study was rancher.

The most frequent clinical presentations showed fever, chills, headache, vomiting, myalgia and abdominal pain (Croche et al. 2013). The most common clinical manifestations of TBRF in the recent study were classic symptoms (82.6%), followed by classic symptoms plus jaundice and classic symptoms plus photophobia and eosinophilia (8.7%, 8.7%), which is similar to other researches performed in this field. In the study of Moemenbellah-Fard et al. (2009) in western Iran, cases of TBRF was almost characterized by recurring episodes of fever, chills and headache. In the investigation of Arshi et al. (2002) in Ardebil, northwestern Province of Iran, the most prevalent clinical manifestations were fever (93.3%), chills (86.2%) and headache (85.9%). In a study in Montana, all patients had fever and other clinical manifestations co-related with TBRF (such as headache, rash, vomiting and myalgia) (Schwan et al. 2003).

Similar to other countries, TBRF prevalent is frequent in warm months. However, the disease also occurs during the winter (Cutler 2010). In our study, nearly 53.3% were occurred in the summer, and the frequencies were from April to March. Cases of RF are reporting from warm provinces in south of the country as well. In Masoumi-Asl et al. investigation, the peak of the TBRF prevalence was in summer and the disease occurred during all months of the year with the maximum reported from June through November (2009). In the United States, patients were reported during all months of the year: 71% cases were occurred from June to September; the majority of cases diagnosed in July (24%) and August (23%) (Dworkin et al. 2002).

The majority cases of TBRF were reported in the year 2002 and 2003 ( $n=115$ , 41.7%). The trend of the disease was down-

ward in recent years probably due to improving health strategies especially among children and adolescents and particularly in rural areas. This significant trend was also shown in both genders, but the changes of this trend were independent to patients' age.

This disease still has resistant foci of infection, where control can be a major healthcare difficulty. Relapsing fever can be acquired by travelers and transmitted to regions where the disease is not epidemic (Colebunders et al. 1993, Dworkin et al. 2002). After eco-challenges or in association with military training or activities such as camping or caving, provided potential hosts and natural disease ecologic cycles coincide (Sidi et al. 2005, Wyplosz et al. 2005).

Although many would complain this limited disease, impact is not a threat to public health, the lack of consideration of relapsing fever as a potential cause of clinical findings is a cause for concern. According to epidemiological distribution, TBRF is endemic in Canada (southern portion of British Columbia), Mexico, Central and South America, central Asia, Africa, the Mediterranean region, and Russia (Colebunders et al. 1993). These mentioned diseases are mostly reported from areas of war, famine, mass migrations, or overcrowding (Dworkin et al. 2008).

## Conclusion

The distribution of relapsing fever was similar in both male and female genders, but its prevalence showed a reduction in the number of victims by the increase of age. The trend of the changes in prevalence of disease has shown a downward prognosis in recent years probably due to improving health strategies especially among children and adolescents and particularly in rural areas. Our study proved that the epidemiological sections of the disease is consistent with previous reports from other regions, but

further studies are required to assess its epidemiological parts correctly in different areas of our country.

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