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The seven-year longitudinal study on relapsing fever borreliosis in Western Iran

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ABSTRACT

Objective: To determine the epidemiologic and clinical features of tick borne relapsing fever in Kurdistan Province during 2000–2006.

Methods: In this cross-sectional clinic-based study, target group was all population of Kurdistan Province. In order to screen patients based on national protocol we diagnosed cases based on clinical symptoms together with the presence of *Borrelia* in blood smears that are stained with Wright–Geimsa. Positive cases after identifying were treated. Also we completed a questionnaire for all patients. The data were analysed by SPSS for getting descriptive indicators (relative and absolute frequency tables).

Results: The numbers of tick borne relapsing fever cases recorded during 2000 to 2006 were as follows: 14, 8, 17, 36, 22, 10 and 31, respectively. A total of 138 patients (50.8% males, 49.2% females) were studied. The most prevalent clinical manifestations were fever (100%), chills (92.7%) and headache (76.1%). Laboratory tests performed on patients showed the presence of *Borrelia persica* in blood smears. Most of the cases (42%) were in the age group 10–19 years old and 86.2% of them were under 30 years old. Nearly 92% of the patients were resident of the villages. About 37.7% and 25.4% of cases were students and housewives, respectively. Approximately 66% of cases were observed in summer. In 70% of cases, the buildings that they lived in were very old. Cattle or sheep were found in the homes of 89.1% of patients.

Conclusions: Due to the relatively high infection rate and economic consequences of this disease on the person and the community, we should take measures to prevent its prevalence by carrying out educational programs.

1. Introduction

Tick borne relapsing fever (TBRF) or endemic relapsing fever is an acute infectious zoonotic disease and sporadically distributed throughout rural areas of the globe[1,2]. TBRF is characterized by recurrent episodes of fever and a variety of nonspecific signs (such as vomiting, chills, abdominal pain, headache, myalgia and arthralgia), which are related to spirochetemia. It has an incubation period of 4 to 18 (or more) d. The infection is affirmed by

observing the spirochetes (*Borrelia* spp.) on blood smear under a microscope, during one of the periods of fever. TBRF often responds to antibiotic treatment[3–6].

This recurrent febrile illness is reported from Africa, South America, North America, Europe and Asia[2,7–9]. Soft ticks (Acari: Ixodida: Argasidae) perform a major role in transmission of TBRF[10]. *Borrelia* species are transferred to persons via the bite of infected *Ornithodoros* spp. ticks. *Borrelia* spp. alter their surface antigens, causing frequent stimulation of the body immune system by the latest antigen and a pyrexial response by the sick[3,11–13]. *Ornithodoros* spp. have nightly blood-feeding habits and pain-free bites. The *Borrelia* spp. can survive for many years in their long-lived vectors. Attainment of human TBRF is universally limited to the geographical range of the *Ornithodoros* tick vectors. The host reservoirs of *Borrelia*

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are rodents[3,12,13].

In Iran three species of Argasidae including, *Ornithodoros tholozani* (*O. tholozani*) (Figure 1), *Ornithodoros erraticus* (*O. erraticus*) and *Ornithodoros tartakovskyi* are able to transmit the TBRF to humans. Moreover, *Borrelia persica* (*B. persica*), *Borrelia microti*, *Borrelia latyschevi*, and *Borrelia baltazardi* (*B. baltazardi*) are the major causative agents of TBRF in Iran[14]. Among these four species of *Borrelia* in Iran, only *B. persica* and *B. baltazardi* are isolated from the blood smears of sick. *B. baltazardi* is isolated from the blood smear of just one sick with TBRF in Iran[15]. *B. persica* is transmitted by *O. tholozani*, *Borrelia microti* and *O. erraticus* which is found in rodent burrows[1]. Lyme borreliosis is recognized as the most common vector-borne human diseases in the northern moderate zone of the globe. Meanwhile, TBRF and Crimean Congo hemorrhagic fever are the most prevalent tick-borne illness in Iran[12,14]. In Iran, principal foci of TBRF are mountainous provinces of north-west and west, and also it is reported from various parts situated in south and center of the country (Figure 2) [1,2,13]. The objective of this research was to determine the epidemiologic and clinical features of TBRF in Kurdistan Province during 2000–2006.



Figure 1. Dorsal view of *O. tholozani*.

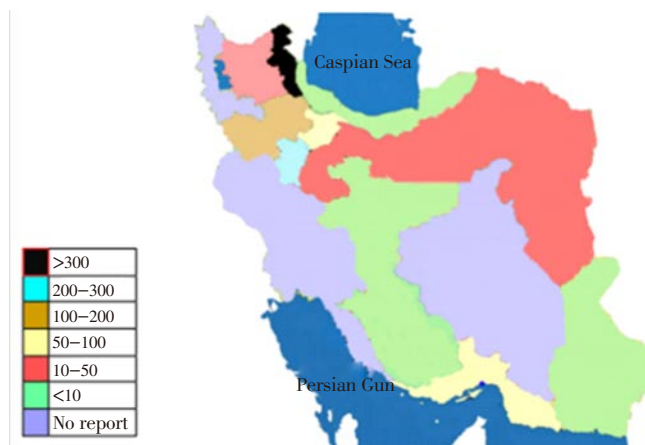


Figure 2. Distribution about the number of infected TBRF in Iran during 1997–2006[2].

2. Materials and methods

The province of Kurdistan is an entirely mountainous area

with 28817 km². It is situated in the west of Iran (Figure 3) and border Iraq on the west, the provinces of Kermanshah to its south, Zanzan to the northeast, Hamedan to the east and West Azerbaijan to the north. The geographical coordinates of this province are from 34°44' to 36°30' of northern latitude and from 42°31' to 48°16' of eastern longitude. Winters are lengthy and can be so cold with heavy snowfalls.



Figure 3. Kurdistan Province in Western Iran.

This study is a field and experimental investigation. This research was done as a cross-sectional and descriptive design. A questionnaire was planned in this study which contained data on clinical manifestations, construction matters, job, distance of livestock from human dwelling place, age, month, season, family size, place of residence, and other related data collected in interviews. Diagnosis was based on clinical symptoms in febrile illness plus the detection of spirochetes (*Borrelia* spp.) under Wright-Giemsa staining in thin and thick blood smears using dark-field microscopy (Figure 4).

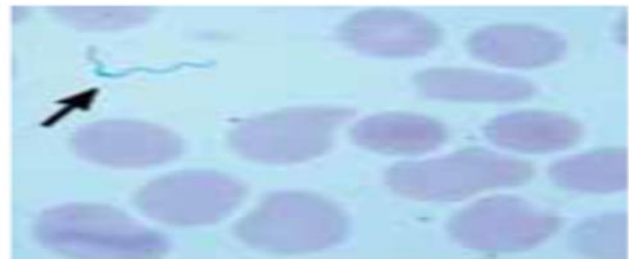


Figure 4. A *Borrelia* spp. spirochete in a smear of peripheral blood.

3. Results

In this epidemiological study, a total number of 138 cases have been found over seven years (2000–2006). The majority cases of TBRF was reported in the year 2003 ($n=36$) (Figure 5). The patients included 50.7% women and 49.3% men. Patients were observed during eight months of the above mentioned years: 114 (82.6%) patients occurred from July through October; most patients were reported in July (37 cases, 26.8%) and August (28 cases, 20.3%) (Figure 6). The highest of patients were diagnosed during the summer and autumn months (Figure 7). The most common clinical symptoms were fever (100%), chills (92.7%), headache (76.1%), sweating (60.9%) and abdominal pain (58%). All cases had fever and other clinical symptoms in accordance with TBRF. Other findings

included vomiting, myalgia, arthralgia, nervousness, cough, photophobia and nose bleeding (Figure 8).

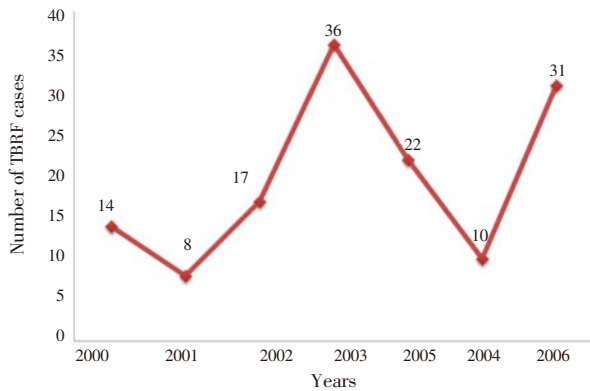


Figure 5. Number of TBRF cases of different years in Kurdistan Province, Western Iran (2000–2006).

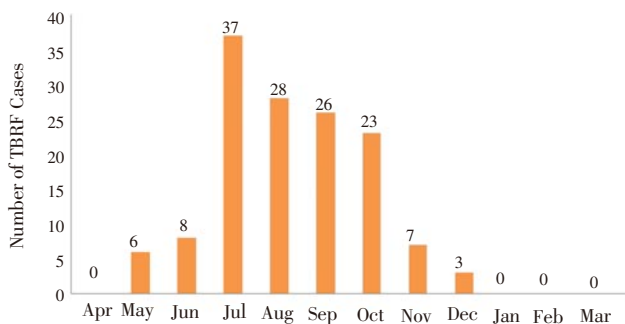


Figure 6. Number of TBRF cases by months in Kurdistan Province, Western Iran (2000–2006).

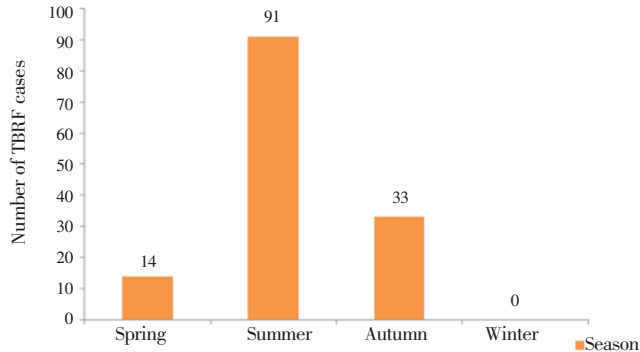


Figure 7. Number of TBRF cases by seasons in Kurdistan Province, Western Iran (2000–2006).

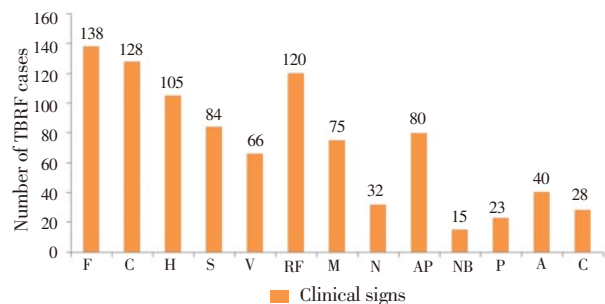


Figure 8. Number of TBRF cases by clinical manifestations in Kurdistan Province, Western Iran (2000–2006).

F: Fever; C: Chills; H: Headache; S: Sweating; V: Vomiting; RF: Recrudescence fever; M: Myalgia; N: Nervousness; AP: Abdominal pain; NB: Nose bleeding; P: Photophobia; A: Arthralgia; C: Cough.

Among about 113 (81.9%) of patients, the houses they

inhabited in were mud-thatched and old; 25 (18.1%) had new brick made houses. Meanwhile, nearly 92% of the patients of TBRF were residents of the villages or were infected during their stay in a village. The disease of TBRF was normally observed in cases less than 30 years old (86.2%, $n=119$). There were 21 patients (15.2%) of the cases less than 5 years old, 58 cases (42%) were 10–19 years old and 28 cases (20.3%) were 20–29 years old (Figure 9). Out of the 138 cases of TBRF, the jobs in 52 (37.7%) and 35 (25.4%) patients were students and housewives, respectively (Figure 10). Approximately 27 (19.6%) of the patients were children who did not work beyond their dwelling places. More than 85.5% of the patients lived in big families (4 or more individuals in family) (Figure 11). About 14.5% of patients was informed that they had been bitten by ticks. Cattles or sheep were kept in the homes of 81.9% of patients ($n=113$). Nearly 61.6% of those cases lived within 10 m far away from the place of livestock (Figure 12).

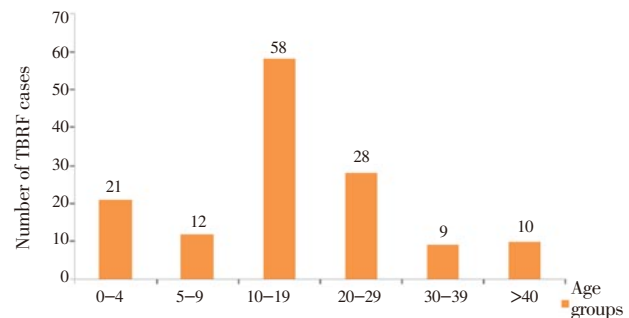


Figure 9. Number of TBRF cases by age groups in Kurdistan Province, Western Iran (2000–2006).

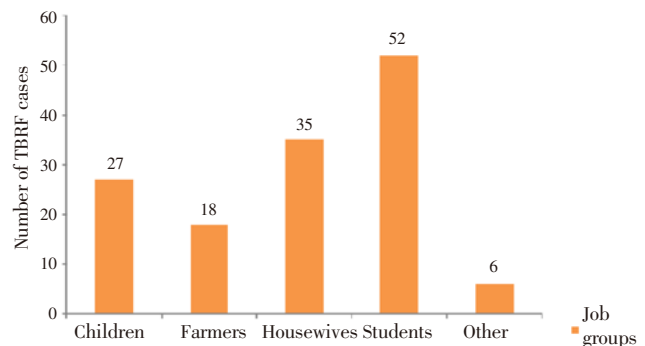


Figure 10. Number of TBRF cases by occupation groups in Kurdistan Province, Western Iran (2000–2006).

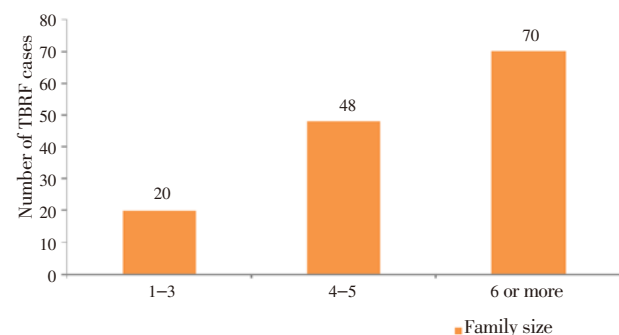


Figure 11. Number of TBRF cases by family size in Kurdistan Province, Western Iran (2000–2006).

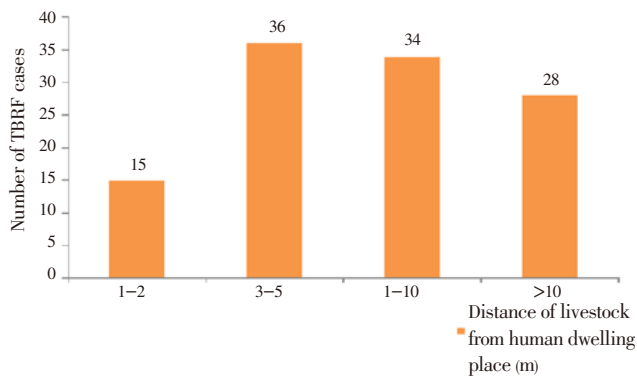


Figure 12. Number of TBRF cases by distance of livestock from human dwelling place in Kurdistan Province, Western Iran (2000–2006).

4. Discussion

TBRF disease is endemic in the Central and Southern America, the western United States, the plateau regions of Mexico, Southern British Columbia throughout most of Africa, central Asia and the Mediterranean[3]. This survey updates the epidemiology of TBRF in the Kurdistan Province, Western Iran. TBRF is endemic in this province. For the first time, *B. persica* was isolated 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 out in Iran in 1879 and after that by named *O. tholozani* Tholozan[1,15]. Many of the TBRF patients are discovered in the provinces situated in Northwestern Iran. Most people in this region are involved into animal husbandry and agriculture jobs. Frequent contacts to the infected ticks are the major reason of great spread of the TBRF.

A study in 1997–2006 in Iran showed that the TBRF was restricted to 18 provinces of the 30 provinces (60% of the provinces). During this period, overall 1415 patients have been found. Ardebil ($n=625$), Hamadan ($n=218$), Zanjan ($n=182$), Kordestan ($n=139$) and Qazvin ($n=66$) Provinces contained 87% of all patients. Other provinces including Hormozgan ($n=53$), Semnan ($n=42$), Tehran ($n=26$), Khorasan ($n=25$), East Azerbaijan ($n=13$), Markazi ($n=11$), Mazandaran ($n=3$), Gilan ($n=3$), Gom ($n=3$), Golestan ($n=2$), Fars ($n=2$), Isfahan ($n=1$) and Siatan–Baluchistan ($n=1$) were comprised 13% of all cases[2].

In this epidemiological survey, the entire cases were treated by appropriate antibiotics. No cases died due to the disease. A total number of 138 cases (50.7% females, 49.3% males) were investigated. In the study of Masoumi–Asl *et al.*, the TBRF cases included 55% women and 45% men[2]. In a study in the United States from 1997 to 2000, the patients comprised 235 men (52%) and 178 women (40%); data regarding gender was missing for 37 (8%)[3]. In the survey

of Arshi *et al.* in Ardabil Province, Iran, a total of 391 (49% females, 51% male) patients were studied from 1998–2001[15]. The most common clinical manifestations of TBRF in the present study were fever (100%), followed by chills and headache (92.7%, 76.1%), which is similar to other researches performed in this field. In the investigation of Arshi *et al.* in Ardabil, northwestern province of Iran, the most prevalent clinical symptoms were reported fever (93.3%), chills (86.2%) and headache (85.9%)[15]. In a study in Montana, all patients had fever and other clinical manifestations consistent with TBRF (such as, headache, rash, vomiting and myalgia)[6]. In the investigation of Moemenbellah–Fard *et al.* in western Iran, cases of TBRF is characterized by recurring episodes of fever, chills and headache[16].

The majority of cases in our study were students and housewives, which is similar to the finding of Rafinejad *et al.* on TBRF in Kurdistan province, western Iran. In the mentioned study, the rates of infection in students, housewives, farmers, children and other were reported 40%, 24.8%, 20.6% and 4.2% respectively[13]. These information represented that all job groups are at risk of obtaining infection. Most of patients in the study of Arshi *et al.* were children[15]. In the present survey, only 14.5% of patients knew that they had been bitten by ticks. A short blood–feeding period (1 to 20 min), a nearly painless bite and a tendency to nightly feeding by *Ornithodoros* ticks are likely to describe why very few individuals reported a history of a bite. In this investigation, 92% out of 138 diagnosed patients of TBRF were found in rural regions and 8% of them were from cities. In study about TBRF from Iran during 1997–2006 approximately 92% of the patients were living in villages that is consistent with our report[2]. In the investigation of Arshi *et al.* more than 84% of the cases were resident of the rural areas or became infected during their stay in a village[15]. In the survey of Rafinejad *et al.*, about 90.7% and 9.3% of cases were occurred in rural and urban areas, respectively[13].

Similar to other countries, TBRF occurs frequently in warm months. However, the disease also occurs during the winter[17]. In our study, nearly 65.9% occurred in the summer, and the frequencies were higher from July to October. In the investigation of Masoumi–Asl *et al.*, the peak of the TBRF occurred in summer and the disease occurred during all months of the year with the maximum reported from June to November[2]. In the study of United States, patients were found during all months of the year; 71% cases occurred from June to September; the majority of cases were diagnosed in July (24%) and August (23%) [3]. In the present study, 81.9% of patients lived in an old building. In the survey of Arshi *et al.*, most (70%) of the subjects lived in the old mud–and–thatch houses[15].

Incidence of the disease was 58%, 28% and 21% among the age groups of 10–19 years old, 20–29 years old and 0–4 years old, respectively. In the study of Rafinejad *et al.*, most frequencies of TBRF based on age groups showed 43.3%, 17.5% and 17.5% in 10–19 years old, 20–29 years old and 0–4 years old, respectively^[13]. In the investigation of Moemenbellah–Fard *et al.*, most (91%) of the patients were reported to be young people^[16]. Masoumi–Asl *et al.* 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^[2]. Approximately 75.2% of the subjects lived within 10 m far away from the site of livestock. Rafinejad *et al.* reported that about 72% of the cases habited within the mentioned distance of livestock^[13]. Results of this survey showed that families lived 1–2 m far away from livestock dwellings had the minimum infection rate, which is similar to the results of Rafinejad *et al.*^[13]. Prevention of TBRF disease comprises avoiding tick and rodent infested places (*i.e.* caves and animal shelters). Furthermore, 50.7%, 34.8%, and 14.5% of *Borrelia* spirochetes infections were detected in family sizes of ≥ 6 , 4–5, and 1–3 person in a family, respectively. This is in accordance with the survey of Rafinejad *et al.*^[13].

TBRF disease should take into consideration the recrudescence febrile illness, and also stained peripheral thin and thick blood smears in the cases should be checked for *Borrelis* spp.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

- [1] Aghighi Z, Assmar M, Piazak N, Javadian E, Seyedi Rashti MA, Kia EB, et al. Distribution of soft ticks and their natural infection with *Borrelia* in a focus of relapsing fever in Iran. *Iranian J Arthropod–Borne Dis* 2007; **1**(2): 14–18.
- [2] Masoumi Asl H, Goya MM, Vatandoost H, Zahraei SM, Mafi M, Asmar M, et al. The epidemiology of tick–borne relapsing fever in Iran during 1997–2006. *Travel Med Infect Dis* 2009; **7**: 160–164.
- [3] Dworkin MS, Shoemaker PC, Fritz CL, Dowell ME, Anderson DE Jr. The epidemiology of tick–borne relapsing fever in the United States. *Am J Trop Med Hyg* 2002; **66**(6): 753–758.
- [4] Dworkin MS, Schwan TG, Anderson DE Jr. Tick–borne relapsing fever in North America. *Med Clin North Am* 2002; **86**: 417–433.
- [5] Wilske B, Johnson BJ, Schrieffer ME. *Borrelia*. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Tenover RH, editors. Manual of clinical microbiology. Washington DC: American Society for Microbiology Press; 2007, p. 746–758.
- [6] Schwan TG, Policastro PF, Miller Z, Thompson RL, Damrow T, Keirans JE. Tick–borne relapsing fever caused by *Borrelia hermsii*, Montana. *Emerg Infect Dis* 2003; **9** (9): 1151–1154.
- [7] Rebaudet S, Parola P. Epidemiology of relapsing fever borreliosis in Europe. *FEMS Immunol Med Microbiol* 2006; **48**(1): 11–15.
- [8] Schwan TG, Anderson JM, Lopez JE, Fischer RJ, Raffel SJ, McCoy BN, et al. Endemic foci of the tick–borne relapsing fever spirochete *Borrelia crocidurae* in Mali, West Africa, and the potential for human infection. *PLoS Negl Trop Dis* 2012; **6**(11): e1924.
- [9] Diatta G, Souidi Y, Granjon L, Arnathau C, Durand P, Chauvancy G, et al. Epidemiology of tick–borne borreliosis in Morocco. *PLoS Negl Trop Dis* 2012; **6**(9): e1810.
- [10] Cunha BA. *Tick–borne infectious disease. Diagnosis and management*. New York: Marcel Dekker Inc.; 2002.
- [11] Dennis DT, Campbell GL. *Relapsing fever*. In: Braunwald E, Hauser SL, Fauci AS, Longo DL, Kasper DI, Jameson JL, editors. *Harrison's principles of internal medicine*. New York: McGraw–Hill; 2001.
- [12] Cutler SJ. Possibilities for relapsing fever reemergence. *Emerg Infect Dis* 2006; **12**(3): 369–374.
- [13] Rafinejad J, Shemshad K, Banafshi O. Epidemiological study on tick–borne (Acari: Argasidae) relapsing fever in Kurdistan Province, Iran, 2000–2004. *Fla Entomol* 2012; **95**(3): 758–763.
- [14] Vatandoost H, Ghaderi A, Javadian E, Nia AZ, Rassi Y, Piazak N, et al. Distribution of soft ticks and their infection with *Borrelia* in Hamadan Province, Iran. *Iranian J Publ Health* 2003; **32**(1): 22–24.
- [15] Arshi S, Majidpoor A, Sadeghi Homayoun ED, Asmar M, Emdadi D, Derakhshan MH. Relapsing fever in Ardabil, a northwestern province of Iran. *Arch Iranian Med* 2002; **5** (3): 141–145.
- [16] Moemenbellah–Fard MD, Banafshi O, Rafinejad J, Ashraf H. Tick–borne relapsing fever in a new highland endemic focus of western Iran. *Ann Trop Med Parasitol* 2009; **103**(6): 529–537.
- [17] Cutler SJ, Bonilla EM, Singh RJ. Population structure of east African relapsing fever *Borrelia* spp. *Emerg Infect Dis* 2010; **16**(7): 1076–1080.