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# Epidemiological characteristics of human brucellosis in Hamadan Province during 2009–2015: results from the National Notifiable Diseases Surveillance System



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### ABSTRACT

*Background:* Human brucellosis and recurrent brucellosis is an ever-increasing public health concern, especially in endemic areas like Iran. Nevertheless, little is known regarding the epidemiology and determinants of recurrent brucellosis. Therefore, the objective of this study was to investigate epidemiological patterns and potential determinants of recurrent brucellosis in Hamadan Province during the years 2009–2015.

*Methods:* Data on reported cases of new and recurrent brucellosis from 2009 to 2015 were obtained from the provincial Notifiable Diseases Surveillance System at Hamadan University of Medical Sciences. Incidence rates per 100 000 were estimated at the county level. Binary logistic regression was used to estimate the effects of background characteristics and recurrent brucellosis. The power of discrimination of the model for recurrent brucellosis was assessed using the area under the curve (AUC).

*Results*: Among 7318 brucellosis cases, the total frequency (%) of recurrent cases was 472 (6.45%). The rate of recurrent brucellosis was higher in females, people aged 50 years and over, people with a history of consuming unpasteurized dairy products with no history of contact with animals, and in the winter season. Multivariable logistic regression analysis showed that female sex (adjusted odds ratio (AOR) 1.36, 95% confidence interval (CI) 1.13–1.65), age  $\geq$ 55 years (AOR 4.15, 95% CI 2.32–7.42), consumption of unpasteurized dairy products (AOR 1.16, 95% CI 0.96–1.40), and winter season (AOR 1.32, 95% CI 1.03–1.71) are potential risk factors for recurrent brucellosis. The final model that involved all the determinants showed moderate discrimination (AUC 0.61).

*Conclusions:* Female sex, older age, and winter months were found to be significant determinants of recurrent human brucellosis. Enhanced surveillance systems with an emphasis on these population characteristics will allow effective preventive and protective measures to be implemented and might alleviate the recurrence of brucellosis in the country.

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# Introduction

*E-mail addresses:* shahrzadnema@yahoo.com (S. Nematollahi), aubi65@gmail.com (E. Ayubi), man.karami@yahoo.com (M. Karami), salmn.khazaei61@gmail.com (S. Khazaei), masoud123@yahoo.com (M. Shojaeian), rezazamani@gmail.com (R. Zamani), kamyarmansori@yahoo.com (K. Mansori), bhzdgholami80@yahoo.com (B. Cholamaliee). Brucellosis is a chronic infectious bacterial disease affecting various species of domestic and wild animals, as well as humans (AlDahouk et al., 2003). It may cause a wide spectrum of clinical symptoms in humans, from a mild flu-like illness to severe disease (Galińska and Zagórski, 2013). The disease is also known to cause serious clinical complications with involvement of the internal

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organs, including encephalitis, meningitis, spondylitis, arthritis, endocarditis, orchitis, and prostatitis (Khan et al., 2001).

The transmission of Brucella most often occurs as a result of contact with animals or their products (through the consumption of unpasteurized milk and dairy products, herding, and lambing) and via occupational contact (e.g., veterinarians, slaughterhouse workers, and farmers) (Husseini and Ramlawi, 2004; Kozukeev et al., 2006; Hasanjani-Roushan et al., 2004). Seropositivity for Brucella has also been shown to increase with age and to be increased in females (Cetinkaya et al., 2005).

The ever-changing geographic distribution of the disease has led to the emergence of new foci, which explains the growing scientific interest in human brucellosis as a re-emerging infectious disease (Pappas et al., 2006). Despite the legal requirement to notify cases of brucellosis to the surveillance notification system in most countries, it is still thought of as a disease with many underreported cases (Taleski et al., 2002). Half of the countries with the highest incidence rate for human brucellosis are located in the Middle East region, including Syria, Turkey, Iran, Iraq, and Saudi Arabia (Pappas et al., 2006). Despite great efforts made by the Ministry of Health, Iran is still considered an endemic area for the disease. However, reports from the National Commission on Communicable Disease Control are promising: the annual incidence of the disease fell from 1000 to 238.6 cases per million population during the years 1989–2003 (Bokaie et al., 2009).

Despite successful therapeutic options proposed by the World Health Organization (Goldsamt et al., 2015), therapeutic failure, recurrence, and a chronic course are characteristic of the disease (Alavi et al., 2009). There is a paucity of evidence regarding risk factors for the acquisition of infection, and evidence regarding risk factors for recurrence is scarce. Recurrence is believed to depend heavily on factors including host characteristics, depressed immunity, type of infection (localized versus systemic), and treatment delays (Alavi et al., 2009). Due to the importance of the management of recurrent brucellosis, epidemiological studies are warranted (Solera et al., 1998). However, the control of human brucellosis requires considerable efforts to build educational infrastructure and establish active surveillance systems (Seleem et al., 2010). Therefore, the identification of the major risk factors for the recurrence of brucellosis is a crucial primary step in reaching a comprehensive understanding of the nature of the disease, and subsequently for the objectives of prevention programs. This study aimed to explore the effect of various risk factors for the recurrence of human brucellosis in the population of Hamadan Province in the west of Iran.

# Methods

# Study area

Hamadan Province is located in the west of Iran and covers an area of approximately 19 493 square kilometers (Figure 1). The province had a population of 1758 268 people in 2011, according to the national census held in that year by the Statistical Center of Iran (https://www.amar.org.ir/english). The main occupation of the people living in the region is animal husbandry (State Government Office, Hamadan, Iran; http://www.ostan-hm.ir/fa/index.aspx? spi=MQ==). Accordingly, many of the people living in Hamadan are at risk of brucellosis. Hamadan Province has nine cities, namely Asadabad, Bahar, Hamadan (center of Hamadan Province), Famenin, Kabudarahang, Malayer, Nahavand, Tuyserkan, and Razan.

# Data sources

Brucellosis is considered a notifiable disease and all cases of brucellosis should be reported to the provincial level section of the

Figure 1. Geographic location of Hamadan Province.

National Notifiable Surveillance System. Data on brucellosis cases caused by *Brucella abortus* and *Brucella melitensis*, recorded at the Department of Health of Hamadan University of Medical Sciences from March 2009 to March 2015, were used in this cross-sectional study. The data collected included sex, age, location (urban/rural), county, time of diagnosis (year and season), type of disease (new case/recurrence case), family history of disease, animal contact history, and history of consuming unpasteurized dairy products. In addition, the population size in 2011 for each county was extracted from the National Census data registered at the Statistics Center of Iran.

According to national guidelines (Iranian Center for Disease Control (ICDC), 2012), a case of brucellosis is defined as a patient with a confirmed clinical diagnosis based on compatible signs and symptoms, a standard tube agglutination test (STA)  $\geq$ 1:80, and 2-mercaptoethanol (2ME) agglutination  $\geq$ 40. In this study, patients who had received at least one full treatment period, but whose symptoms had not improved or had recurred after the treatment had ended, were considered as recurrence cases (Colmenero et al., 1996).

## Statistical methods

The spatial distribution of brucellosis incidence and recurrence rates (%) were depicted using ArcView software. The Chi-square test was used to assess the association between patient demographic characteristics and disease outcomes. Crude and multiple logistic regression models were used, with disease type as the binary dependent variable (new case as a baseline and recurrent case).

The Hosmer and Lemeshow approach was used for model building, and the model was fitted with all variables with a *p*-value less than 0.2. The internal validity of prognostic models was checked through bootstrapping. A multiple logistic regression model including all explanatory variables was constructed to calculate the probability of recurrence and treatment complications, with the discriminant power of all explanatory variables assessed by receiver operating characteristic curve (ROC curve). In a ROC curve, the true-positive rate (sensitivity) is plotted as a function of the false-positive rate (1 – specificity) for different cutoff points of a parameter. The area under the curve (AUC) measures discrimination, i.e., the ability of the test to correctly diagnose each outcome of interest.



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