Epidemiological, Risk Factors, Clinical, and Laboratory Features of Brucellosis in the Southwest of Iran within 2009–2015

Abstract

Background: Brucellosis is a serious disease affecting many individuals in the world and in Iran. The aim of this study was to investigate the epidemiological and clinical features of patients diagnosed with brucellosis in Kohgilouyeh and Boyerahmad province, southwest of Iran. **Methods:** This retrospective descriptive-analytic study included all individuals diagnosed with brucellosis during 2009–2015. The clinical and epidemiological information were gathered from recorded data available in the health center of Kohgilouyeh and Boyerahmad province, the southwest of Iran. **Results:** The total number of patients diagnosed with brucellosis during the study period was 658, of whom, 339 (51.5%) were males. A total of 541 (82.2%) patients resided in rural and tribal areas, and the others lived in urban regions. The mean age of diagnosis was 39.59 ± 17.28 years and the most prevalent age groups were 31–50 (277, 42.1%) and 11–30 (178, 27.1%)-year olds. The most affected groups were housekeeper women (229, 34.8%) and ranchers (152, 23.1%). The relationship between jobs and disease was significant ($P < 0.001$). Transmission through either suspected dairy products (582, 88.4%) or close contact with infected livestock (537, 81.6%) comprised the most common routes of brucellosis dissemination. The clinical presentation was acute in the majority (581, 88.3%) of the patients. The highest titer for both wright and Coombs wright tests was 1:320. The most frequently administrated drugs were doxycycline and streptomycin (183, 27.8%). The most commonly observed clinical symptom was bone pain (477, 72.5%). Arthritis (12, 1.8%) comprised the most frequent drug-associated complication. Either relapse or treatment failure was recorded collectively in four (0.6%) patients. **Conclusions:** Due to the prevalence of the disease in the nomadic areas, timely detection and control of the disease is essential. Furthermore, livestock vaccination along with educating farmers and physicians about brucellosis can be helpful.

Keywords: *Brucellosis, clinical, epidemiology, Iran, risk factors*

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Introduction

Brucellosis is a common infectious disease affecting both humans and animals. The disease may represent with fever, fatigue, sweating, arthritis, and enlargement of the liver and spleen.[1] Nevertheless, the disease has a wide range of clinical manifestations including musculoskeletal, digestive, urogenital, hematological, cardiovascular, respiratory, and central nervous system symptoms.[2] Brucellosis is a major concern for both health and financial facilities in many parts of the world including the Mediterranean, Middle East, as well as countries surrounding Persian Gulf.[3] Accordingly, brucellosis is also one of the most common infectious diseases in many parts of Iran.[4]

According to the data reported by the Iran Ministry of Health [Figures 1 and 2], brucellosis incidence has increased from 12,248 cases in 2010 to 20,117 in 2014, showing an increment of 70% in this period. The reasons behind this raise are controversial and multifactorial. A major factor may be reduction in domestic production of brucellosis vaccine in the Razi Vaccine and Serum Research Institute. In addition, reduced or halt of vaccine supply from international companies due to political sanctions can also be a potential reason. This notion is supported by declination of brucellosis incidence during 2015–2016 when vaccination was resumed as sufficient products were available.

Vaccination and surveillance of brucellosis among animals are necessary to prevent the transmission of the disease to humans.[5,6] In addition to this, appropriate and accurate epidemiological and clinical data are required to implement effective preventive

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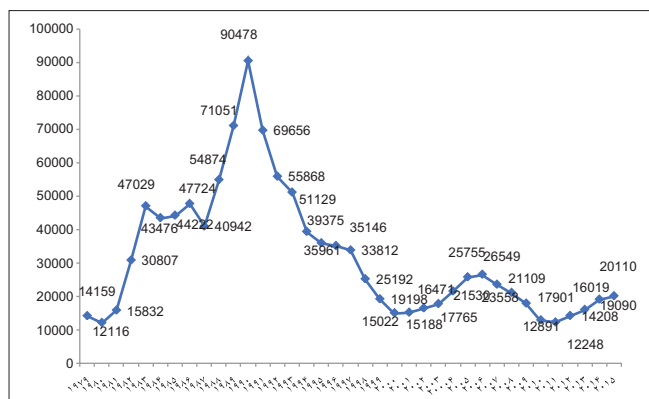*E-mail: hdyt.jamali@yahoo.com*

Figure 1: The incidence rate of brucellosis in Iranians from 1979 to 2015. Horizontal axis denotes the time period in years and the vertical axis shows the incidence rate per 100,000 population (adapted from Iranian Health Ministry report; http://www.health.gov.ir)

and therapeutic policies for brucellosis.[7] Brucellosis has been a serious health-care concern in Iran with multiple reports on its severe complications.[8-10] Some risk factors of brucellosis in Iranian population have been unprotected animal contact and using nonpasteurized dairy products.[10] There is incomplete knowledge about the epidemiological and clinical aspects of brucellosis, especially among rural and tribal populations of Iran. Accordingly, we found no previous reports on brucellosis epidemiology in Kohgilouyeh and Boyerahmad province in the southwest of Iran except for one epidemiological report conducted within 2009–2013.[11] There were significant differences in the geographic distribution of brucellosis, with the incidence rates being highest in most of the cities in the west and north-west of the country.[12] Here, we aimed to provide a comprehensive view on the epidemiological and clinical features of patients with brucellosis in this area during 2009–2015. This study can be complementary to the previously published data.

Methods

In this retrospective descriptive-analytic study, all the cases of brucellosis whose data were available at the Kohgilouyeh and Boyerahmad (Yasouj) health center were included. The demographic, clinical, and laboratory information of the patients were acquired. Our study was conducted according to the ethical consideration of the Declaration of Helsinki 2000 revision.

Diagnosis of brucellosis

Brucellosis was diagnosed based on the relevant clinical picture (i.e., intermittent or persistent fever, fatigue, anorexia, and weight loss) along with confirmatory laboratory results including the detection of agglutinating antibodies (wright, Coombs wright, and 2-mercaptoethanol [2-ME] tests) and/or a positive blood culture test. The thresholds of the serological tests for being considered as positive were ≥1:80 and ≥1:40 for wrights and 2-ME tests, respectively. Coombs wright test was considered positive if agglutination was observed in

three dilutions prior to the observed wright titer (e.g., for a wright titer of 1:80, a Coombs wright of 1:40 would be positive). A blood culture was rendered as a confirmatory test in case of positivity for any brucellosis strains.[13,14] Based on these criteria, 658 patients were diagnosed with brucellosis during the time course of the study.

Inclusion and exclusion criteria

The patients diagnosed with brucellosis according to the previously mentioned criteria during 2009–2015 who were residents of Kohgilouyeh and Boyerahmad province were included. They all had been registered in our local system of reporting and management of diseases.

Statistical analysis

The data were analyzed using SPSS 19 software. Descriptive statistics (means and frequencies) were used to present the population's characteristics. The Chi-square and independent sample Student *t*-test were applied for seeking any relationship or significant differences between different groups. A two-tailed *P* value of less than 0.05 was considered as statistically significant.

Results

Out of 658 patients diagnosed with brucellosis during 2009–2015, 339 (51.5%) and 319 (48.5%) were males and females, respectively. A total of 541 (82.2%) cases were residents of rural and nomadic areas, whereas 117 (17.8%) patients lived in urban areas. The mean age of brucellosis diagnosis was 39.59 ± 17.28 years which was significantly different between men (40.81 ± 18.33 years) and women (38.30 ± 16.30 years) (*P* < 0.001, Table 1). The relationship between jobs and disease was significant (*P* < 0.001). The most prevalent titer for wright test was 1:320 (24%). The results of Coombs wright, 2-ME, and blood culture tests have been presented in Table 2.

The time-lapse from diagnosis to cure was 0–3 months for 581 (88%) cases (corresponding to acute brucellosis). In additions, this period was 3–12 months for 64 (9.7%) patients (representing subacute brucellosis). For 13 (2%) patients, the period exceeded from 1 year, suggesting chronic brucellosis. Due to the variable clinical picture of the disease, final diagnosis was delayed in a number of patients until confirmatory laboratory results received. A family history of brucellosis was recorded in 40 (11.8%) and 38 (11.9%) of male and female patients, respectively (*P* = 0.36) [Table 3].

There were 45 different combinations of administrated therapeutic regimens. The most commonly prescribed drugs were doxycycline and rifampin [Table 4]. Furthermore, rifampin was the first-line drug in relapsed patients. The majority of the patients (84.6%) did not experience any adverse drug reactions. Others, however, encountered arthritis (9, 1.4%), encephalitis (1, 0.2%), arthritis and spondylitis (2, 0.3%), and other reactions (6, 0.9%).
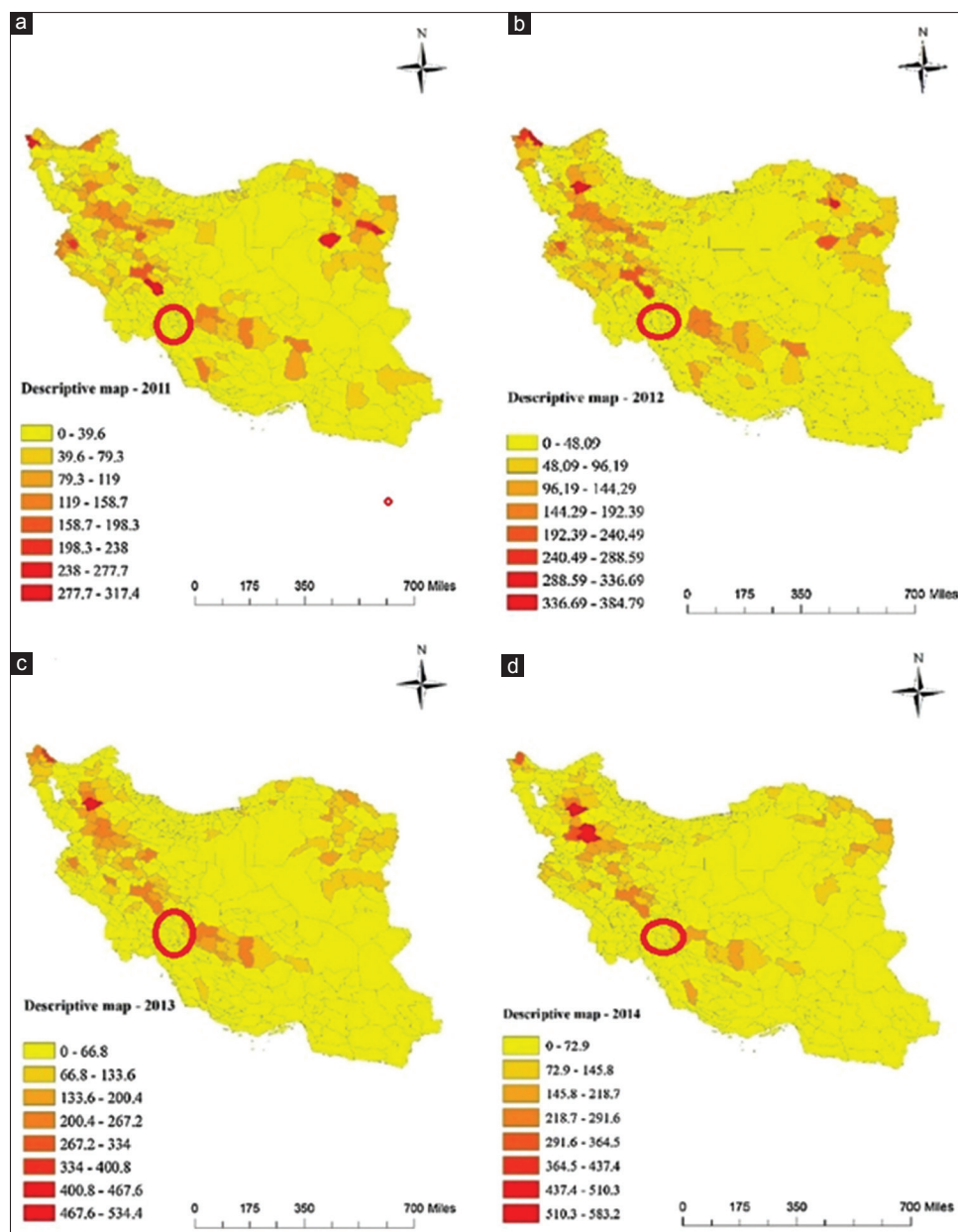
Figure 2: (a-d) Distribution of brucellosis incidence rate in different geographical regions of the Islamic Republic of Iran during 2011-2014 (Kohgilouyeh and Boyerahmad province is marked with a red circle, adapted from Pakzad *et al*.[12]

The peak incidence of brucellosis was in spring and summer (460, 70%, Figure 3).

Discussion

In the present report, the clinical and epidemiological aspects of brucellosis were assessed in Kohgilouyeh and Boyerahmad province, the southwest of Iran during 2009–2015. The general knowledge and public awareness about brucellosis are low among Iranians.[15] Brucellosis is a common infectious disease in many regions of the world. The incidence of brucellosis has increased in developing countries during recent years.[6]

Accordingly, the incidence rate of brucellosis has increased in recent years in Iran with the peak incidence in the northwest and northeast regions.[12] In fact, the countries with the highest incidence rate of brucellosis in the Middle East are Saudi Arabia, Iran, Palestine, Syria, Jordan, and Oman.[16] Accordingly, we here observed a respectively high prevalence of brucellosis in our province.

Out of 658 patients identified during 2009–2015, males constituted 51.5% of the cases. This ratio was similar to previous studies performed in Iran (49.5–54.2%),[11,17] Turkey (55.7%),[18] and Saudi Arabia (66.5%).[19] On the contrary, women constituted the majority of patients with brucellosis in some other reports (59%).[20] The mean age of brucellosis diagnosis was 39.59 ± 17.28 years in our study, which was similar to previous studies in

Table 1: Epidemiological and clinical findings in 658 patients with brucellosis in Kohgilouyeh and Boyerahmad province, Southwest of Iran

Variables			Male	Female	*P*
Age of diagnosis (mean±SD)			40.81±18.33	38.30±16.30	<0.001
Occupation		Rancher	152 (23.1%)		<0.001
		Housekeeper	229 (34.8%)		
		Farmer and rancher	95 (14.4%)		
		Housewife and rancher	14 (2.1%)		
		Student	51 (7.8%)		
		Collegian	2 (0.3%)		
		Farmer	5 (0.8%)		
		Self-employment	6 (0.9%)		
		Employee	16 (2.4%)		
		Manual worker	17 (2.6%)		
		Children	21 (3.2%)		
		Other	50 (7.6%)		
Clinical symptoms	Yes	Fever	434 (66)		0.001
	No		224 (34)		
	Yes	Fatigue and anorexia	275 (41.8)		0.672
	No		383 (58.2)		
	Yes	Backache	366 (55.6)		0.383
	No		291 (44.2)		
	Yes	Musculoskeletal and bone pain	477 (72.5)		0.04
	No		181 (27.5)		
	Yes	Weight loss	180 (27.4)		0.761
	No		478 (72.6)		
	Yes	Depression	5 (0.8)		0.703
	No		653 (99.2)		
	Yes	Weakness and lethargy	61 (9.3)		0.878
	No		597 (90.7)		
	Yes	Adenopathy, hepatosplenomegaly	2 (0.3)		0.966
	No		656 (99.7)		
Local climate		Cool	232 (35.3)		0.287
		Tropical	426 (64.7)		
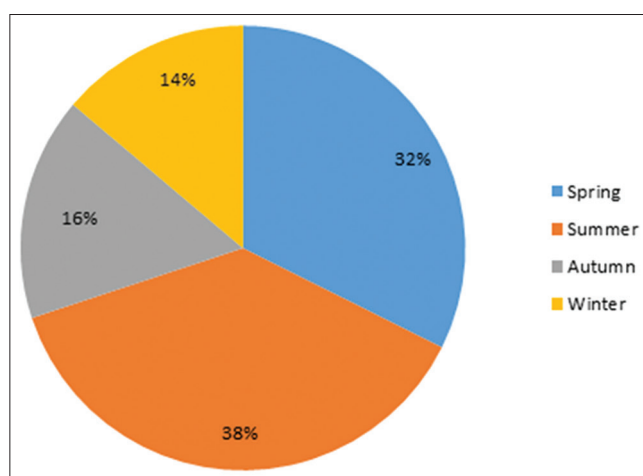
Figure 3: The seasonal incidence of brucellosis in Kohgilouyeh and Boyerahmad province, southwest of Iran

Iran.[9,17] There were also studies in which the mean age of brucellosis diagnosis was higher compared to our study.[2,18,19] In this study, brucellosis was more prevalent in the 31–50-year-old age group. In comparison, the age groups of 15–20[21] and 40–49 years have been noted as the most common age groups affected with brucellosis in precedent reports.[18] Overall, brucellosis is a disease affecting both genders and a wide range of age groups necessitating preventive measures to be implemented throughout the populations.

Similar to a study by Moosazadeh *et al.*,[10] we found that brucellosis was more common among housewives, ranchers, and farmers. The disease was also more prevalent in the tropical regions of the province compared to the cold regions. Furthermore, brucellosis incidence was reported in all the seasons; however, it was more prevalent in spring and summer corresponding to livestock breeding and lactation periods. This pattern of distribution has also been described in previous studies in Iran and overseas.[17,21] It is recommended for at-risk individuals to consider appropriate cautious measures when contacting with livestock, especially in breeding and lactation seasons.

Table 2: Laboratory test results in 658 patients with brucellosis in Kohgilouyeh and Boyerahmad province, Southwest of Iran

Variables		Brucellosis patients (*n*=658) *n* (%)	*P*
Wright test*	1:40	15 (2.3)	0.376
	1:80	74(11.2)	
	1:160	135(20.5)	
	1:320	158(24)	
	1:640	102(15.5)	
	1:1280	128(19.5)	
	Unknown	46(0.7)	
Coombs wright test*	1:40	12(1.8)	0.251
	1:80	16(2.4)	
	1:160	45(6.8)	
	1:320	57(8.7)	
	1:640	31(4.7)	
	1:1280	26(4)	
	Unknown	471(71.6)	
2-ME*	1:20	10(1.5)	0.845
	1:40	60(9.1)	
	1:80	122(18.5)	
	1:160	72(10.9)	
	1:320	62(9.4)	
	1:640	43(6.5)	
	1:1280	4(0.6)	
	Unknown	285(43.3)	
Blood culture	Performed	17(2.6)	0.551
	Unknown	641(97.4)	

2-ME=2-Mercaptoethanol. *The thresholds for positive serological tests were as ≥1:80 and ≥1:40 for wrights and 2-ME tests, respectively. Coombs wright test was considered positive if it rendered agglutination in three dilutions behind the wright test (e.g., for a wright of 1:80, a Coombs wright of 1:40 was described as positive)

Table 3: Risk factors in 658 patients with brucellosis in Kohgilouyeh and Boyerahmad province, Southwest of Iran

Potential risk factors		Brucellosis patients *n*=658		*P*
		Male *n*=339 *n* (%)	Female *n*=319 *n* (%)	
Contact with livestock	Yes	275 (81.1)	262 (82.1)	0.16
	No	64 (18.9)	54 (16.9)	
	Unknown	0 (0)	3 (0.9)	
Consumption of suspected dairy products	Yes	301 (88.8)	281 (88.1)	0.86
	No	36 (10.6)	35 (11)	
	Unknown	2 (0.6)	3 (0.9)	
Family history of brucellosis	Yes	40 (11.8)	38 (11.9)	0.36
	No	269 (79.4)	242 (75.9)	
	Unknown	30 (8.8)	39 (12.2)	
Animal vaccination	Yes	190 (56)	155 (48.6)	0.10
	No	96 (28.3)	95 (29.8)	
	Unknown	52 (15.3)	65 (20.4)	
	No nearby animals	1 (0.3)	4 (1.3)	

The most prevalent clinical manifestations of brucellosis were fever, anorexia, weight loss, low back, and muscle pains. These were also common clinical features reported in a previous study.[16] In addition, anemia has been described as a common clinical finding in patients with brucellosis in precedent studies from Iran[4] and other countries.[3,5] Due to the high clinical variability of brucellosis, the final diagnosis may be delayed if appropriate and timely confirmatory laboratory evidences are not warranted. In a number of our patients, the final diagnosis and therefore therapeutic measures were delayed due to the late development of clinical symptoms and procrastinating in obtaining confirmatory laboratory tests. Therefore, physicians should be prompted to order appropriate tests in suspicious individuals.

The consumption of unpasteurized dairy products as well as close contact with infected livestock were the most common routes for brucellosis transmission in our study. This was similar to previous reports in Iran[11] and Turkey.[2] A family history of brucellosis was identified in 18.5% of our cases. However, this ratio was higher in other studies reaching as high as 40% in some reports.[3,6,22] The most common tests utilized to diagnose brucellosis are serological tests (i.e., wright, Coombs wright, and 2-ME). In this study, wright test retrieved positive results in 24% of the patients with the most prevalent titer as 1:320. Furthermore, the majority of our patients represented 1:320 and 1:80 titers for Coombs wright and 2-ME tests, respectively. In comparison, positive wright test was reported in 3.3% of patients with brucellosis in a study performed in Fars province of Iran.[20] In a study in Turkey, 98.8% of 1016 patients with brucellosis showed positive results for the standard tube agglutination Coombs test.[23] In another recent report in Georgia, positive wright test was found in 41% of patients with brucellosis.[24] In comparison, we observed positive STA Coombs, 2-ME, and wright tests in 97 (17%), 363 (55.1%), and 597 (90.7%) of the cases.

In this study, 88%, 9.7%, and 2% of the patients achieved cures within 0–3, 3–13, and >12 months, respectively. These ratios were representatives of acute, subacute, and chronic brucellosis, respectively. Compared to this, 53.6% and 21.5% of patients with brucellosis showed acute and chronic presentations, respectively, in a study performed in China.[25] The outcomes of therapeutic strategies in brucellosis are variable based on the clinical presentations. The selection of appropriate therapeutic regimes is important for nailing effective management of brucellosis. We here observed that doxycycline–streptomycin regime was more effective than doxycycline–rifampin regarding lower adverse effects (29% vs. 10%, respectively) which is in line with a previous report from Spain.[22]

Although 72% of Iranian populations reside in urban areas, the majority of our patients with brucellosis were residents of rural and tribal regions. This finding was in accordance with the observations of other researchers.[10,11,19] A

Table 4: Therapeutic protocols in 658 patients with brucellosis in Kohgilouyeh and Boyerahmad province, Southwest of Iran

Therapeutic combinations	Percentage n=658 n (%)	Duration (weeks)
Doxycycline + rifampin	183 (27.8)	2-8
Doxycycline + streptomycin	84 (13.1)	1-8
Doxycycline + streptomycin + rifampin	54 (8.2)	2-8
Gentamicin + cotrimoxazole	49 (7.4)	2-8
Gentamicin	32 (4.9)	1-2
Cotrimoxazole + rifampin	28 (4.3)	2-8
Rifampin	23 (3.5)	2-8
Doxycycline + gentamicin + rifampin	21 (3.2)	2-8
Tetracycline + rifampin	17 (2.6)	2-8
Gentamicin + rifampin	16 (2.4)	1-4
Streptomycin	12 (1.8)	1-3
Streptomycin + rifampin	10 (1.5)	3-8
Others	129 (19.3)	1-8

considerable ratio of rural and tribal households does animal husbandry for a living, which can partly explain the higher rates of brucellosis in these populations. Educating these at-risk individuals can be a suitable strategy to manage and prevent brucellosis transmission from livestock to humans.

Conclusions

Implementing managemental policies regarding brucellosis requires a comprehensive epidemiological view on the disease. Regarding the prevalence of the disease among young age groups, timely diagnosis of brucellosis is crucial in this active group of societies. Regarding the severe complications and the complex diagnostic and therapeutic aspects of brucellosis, preventive measures are by far more cost-effective in this condition. In addition to vaccination of livestock, teaching farmers to avoid contacting with infected livestock and not to consume nonpasteurized dairy products can be helpful. It is highly recommended to implement a systematic comprehensive health education and promotion model in order to boost general education about brucellosis.

Conflicts of interest

There are no conflicts of interest.

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