

Epidemiological Changes and the Age-Standardized Incidence Trend (ASR) of Brucellosis in Khomein City, Iran (2014-2016)

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ABSTRACT

Brucellosis is associated with low productivity, abortion, disability, and weakness in cattle, as well as a dramatic drop in the economic and social capital of countries. Since Markazi province is considered to be a high-infection region in Iran, the present study aimed to evaluate the epidemiology and incidence trend of brucellosis in Khomein city during 2014-2016. This descriptive-analytical study was conducted in Khomein using the data of the national program of brucellosis. Sample population consisted of patients with brucellosis, whose data were recorded. The age-standardized incidence rate (ASR) of brucellosis was calculated using the world standard population. Data analysis was performed in SPSS version 20. Mean age of the patients was 40.9 ± 19.1 years. During the study, mean annual incidence rate (IR) of brucellosis was 61.8, and mean ASR was estimated at 56.16 per 100,000. Among the patients, 62.7% were male, and 88.7% were rural residents; no significant difference was observed between these variables ($P=0.26$). In terms of occupation status, the majority of the subjects were farmers/ranchers (25.5%) and housewives (18.6%). In addition, the majority of the subjects were in their thirties or sixties. They also had a history of animal contact as a risk factor for brucellosis (87.7%). Muscle pain and back pain (92.6%) were the most common causes of referral. Despite the slow decline in the disease process, Khomein province is among the regions with high rates of infections in Iran. It seems the pattern of the transmission and risk of brucellosis is changing from food to work, which requires the attention of health policymakers to carry out appropriate interventions, such as the proper implementation of the SHEP program, in order to reduce the incidence of brucellosis.

Introduction

Brucellosis is the most prevalent zoonotic disease across the world, which is transmitted from infected animals to humans. Brucellosis is mainly caused by *Brucella abortus*, leading to infertility in men and potential infertility in women [1]. This disease is also referred to as 'raging fever' and 'Mediterranean fever'. *Brucella* is a gram-negative bacillus that is destroyed by boiling and pasteurization. Brucellosis is transmitted through direct contact with livestock and its discharge or the consumption of contaminated dairy products. In humans, the most common cause of brucellosis is *B. melitensis* [2].

Brucellosis is a significant concern in terms of the health, economic, and social aspects since it is associated with low efficiency, abortion, disability, and weakness in livestock, which lead to a dramatic drop in the economic and social capital of countries [3, 4]. This systemic infection has clinical manifestations and nonspecific symptoms. With the exception of tuberculosis and syphilis, no other infectious disease is known to be more clinically diverse than brucellosis [5].

Brucellosis is globally prevalent due to the spread of infections in domestic and wildlife traps [6]. According to reports, the disease has a higher prevalence rate in the Mediterranean, Latin America, and the Middle East (Saudi Arabia, Iran, and Iraq) compared to the other regions in the world [7]. According to the World Health Organization (WHO), approximately 500,000 individuals are affected by brucellosis each year, which accounts for only 20% of the total population [8].

Despite the establishment of active healthcare systems in our country, Iran is ranked fourth in the world and first in the region regarding the incidence of brucellosis [9]. Similar to many developing countries, there is no

accurate data on the annual incidence of brucellosis in Iran. The average annual incidence rate of the disease in Iran was reported to be 43.24 per 100,000 during 1991-2008 [10], while the Department of the Ministry of Commonwealth for the Control of Diseases reported the incidence rate to be 15.9 per 100,000 in 2010 [11].

The incidence of brucellosis varies in different regions. According to the latest report on brucellosis in Iran, the central regions and provinces of Lorestan, Kermanshah, East Azerbaijan, West Azarbaijan, Hamadan, and South Khorasan have high brucellosis rates (41-31 per 100,000), followed by the provinces of Kurdistan, Razavi Khorasan, and Zanjan (30-21 per 100,000) [12].

Brucellosis affects men and women, while it has been reported to be more prevalent in the former [13, 14]. Moreover, several studies have denoted the higher incidence rate of the disease in rural areas compared to urban areas [15]. Therefore, it could be concluded that gender and occupation are the two major risk factors for brucellosis.

Khomein is a city located in the central province in Iran, which is a highly polluted region in the country. On the other hand, due to its border with Lorestan province (high rate of pollution) and common livestock trade and use in the area, Khomein city is considered to be among the high-risk areas for brucellosis in the province.

No prior investigation has been focused on the incidence and epidemiological characteristics of brucellosis in Khomein city. The present study aimed to determine the epidemiological changes and the trend of the occurrence of brucellosis in Khomein during 2014-2016. It is hoped that our findings enable policymakers and healthcare professionals to recognize brucellosis and

apply effective interventions for the reduction, prevention, and control of the disease.

Materials and Methods

This cross-sectional, descriptive-analytical study was conducted using the data of the national program of registration and care of brucellosis, which was implemented during 2013-2016 in Khomein city, Iran. Sample population consisted of patients with brucellosis diagnosed during the study period based on the national guidelines for combating brucellosis. Patients were assessed using the census method.

Data were collected using the standard form of the national brucellosis program (epidemiological survey form for brucellosis). The information of data were recorded monthly by laboratories, private- and public-sector physicians, and health centers. In order to calculate the incidence rate (IR) of brucellosis, the statistical population of the city ($n=100,000$) was determined in 2014, 2015, and 2016. In addition, the standard population was used to calculate the age-standardized incidence rate (ASR) of brucellosis.

Data analysis was performed in SPSS version 20 using descriptive statistics (mean, standard deviation, charts, and frequency distribution

tables) and analytical statistics (independent t-test and Chi-square). In the statistical analyses, P-value of less than 0.05 was considered significant. The study procedures were performed in accordance with the Declaration of Helsinki, and personal data of the patients remained confidential.

Results

During 2014-2016, 204 new cases of brucellosis were reported, with the highest incidence of the disease recorded in 2015 (69.2 per 100,000). During this period, the mean IR of brucellosis was 61.8 cases per 100,000 per year, while the mean ASR was 56.1 per 100,000. In addition, the highest ASR was estimated at 61.6 per 100,000 in 2015 (Figure 1).

During the study period, the IR of brucellosis was 75.4 per 100,000 in men and 47.3 per 100,000 in women, while the ASR was 70.8 and 40.5 per 100,000 in men and women, respectively. Patients were within the age range of 3-89 years with the mean age of 40.9 ± 19.1 years. In total, 62.7% of the patients were male ($n=128$), and 37.3% ($n=76$) were female. Mean age of the male and female patients was 38.9 and 44.3 years, respectively, which showed a significant correlation in this regard ($P=0.052$).

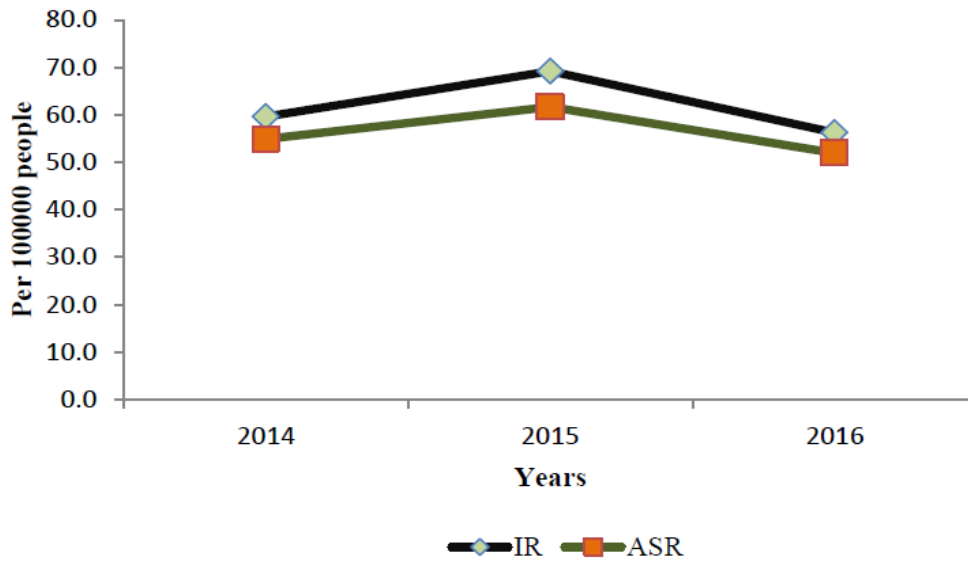


Figure 1. Trend of Incidence Rate of Brucellosis in Khomein City, Iran (2014-2016)

Among the patients, 88.7% lived in rural areas, and 11.3% were urban residents. Mean age of rural and urban residents was 40.2 and 46 years, and the difference in this regard was not considered significant ($P=0.169$). Therefore, the results showed no significant difference in the place of residence and gender with the incidence of brucellosis ($P=0.26$; $X^2=1.23$).

In terms of age distribution, the highest number of the cases with brucellosis was in the age range of 20-29 years (third decade of life) and sixth decade of life, while the lowest frequency was in the age range of 80-89 years (Table 1). In general, the male-to-female ratio was 1.7:1 was obtained, So that the ratio of male to female was obtained five in the age range of 0-9 years.

Table 1. Frequency Distribution of Brucellosis Patients Based on Age and Gender in Khomein Province (2014-2016)

Age Range (year)	Male	Female	N (%)	Male-to-Female Ratio
0-9	5	1	6 (2.9)	5
10-19	17	5	22 (10.8)	3.4
20-29	29	13	42 (20.6)	2.23
30-39	17	11	28 (13.7)	1.54
40-49	18	15	33 (16.2)	1.2
50-59	19	17	36 (17.6)	1.11
60-69	15	7	22 (10.8)	2.14
70-79	7	5	12 (5.9)	1.4
80-89	1	2	3 (1.5)	0.50
Total	128	76	204 (100)	1.7

In terms of occupational status, the majority of the patients with brucellosis were

farmers/ranchers (25.5%) and housewives (18.6%) (Figure 2).

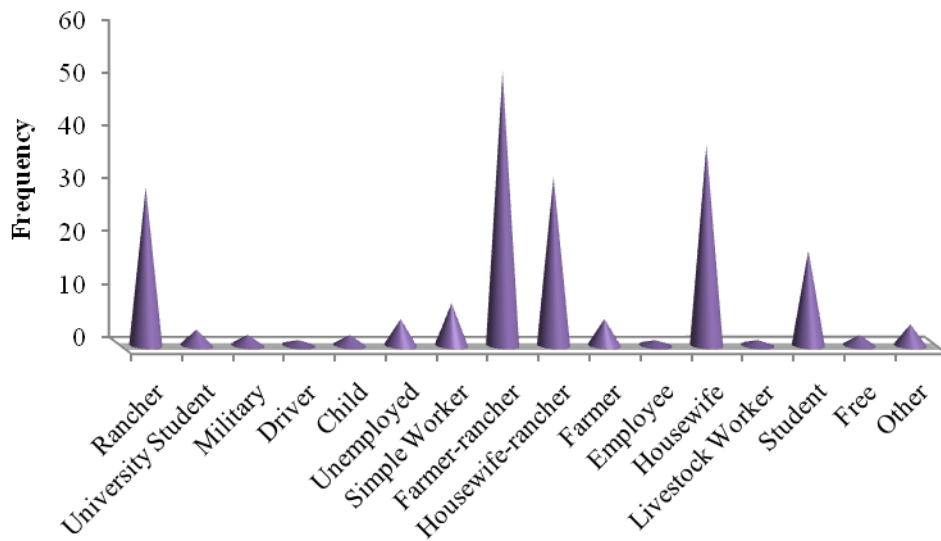


Figure 2. Frequency Distribution of Brucellosis Patients in Terms of Occupation Status in Khomein City, Iran (2014-2016)

The highest prevalence rate of brucellosis was reported in summer (35.3%), and the lowest rate was recorded in winter (14.2%). Among the months of the year, the highest prevalence

rate of brucellosis was reported in July (15.7%) (Figure 3).

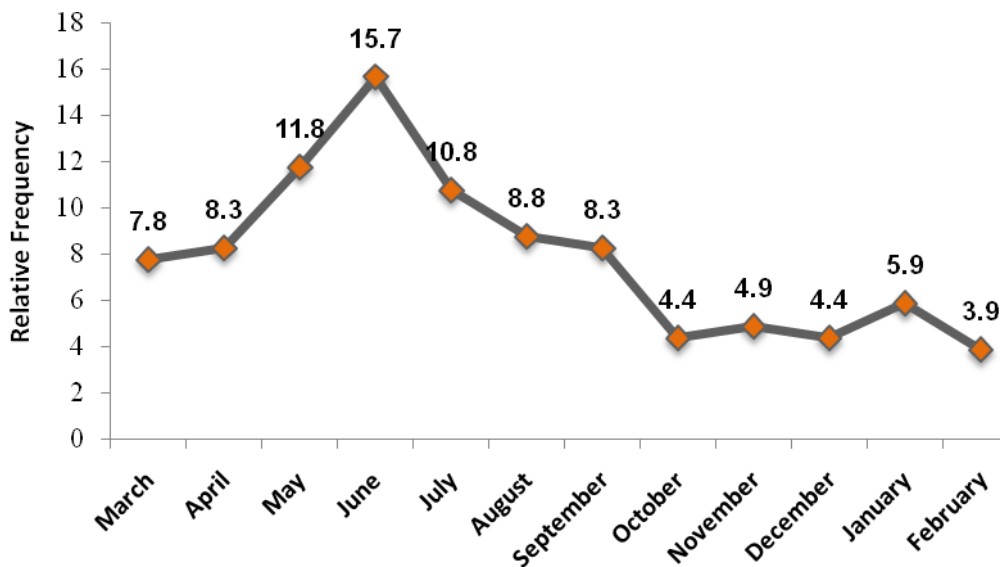


Figure 3. Distribution of Relative Frequency of Brucellosis Cases in Terms of Month in Khomein City, Iran (2014-2016)

According to the results of Wright's test, 42.2% of the patients were in the range of 1/160. In addition, 2ME test showed that titre

1/80 (37.3%) had the highest frequency among the patients. Regarding the history of dairy product consumption, milk consumption

(52%) and cream consumption (25.5%) were the most likely causes of brucellosis transmission, as well as the associated morbidities, in the present study, So, 31.9% of

patients did not use dairy products. Among the patients, 87.7% had a history of contact with livestock, and they kept livestock in their Location near the house (Table 2).

Table 2. Distribution of Relative Frequency of Patients with Brucellosis in Terms of Possible Causes Contributing to Disease Morbidities

Possible Risk Factors	Relative Frequency (%)	Possible Risk Factors	Relative Frequency (%)
History of Dairy Consumption	65.2	Milk Cream Consumption	25.5
Milk Consumption	52	History of Contact with Livestock	87.7
Cheese Consumption	13.7	Keeping Animals in Residence	74.5
Cream Consumption	6.9	Slaughter of Animals, Contact with Blood and Secretions	30.9
Butter Consumption	5.9	Contact with Live Animals	73
Colostrum Consumption	3.4	Presence of Livestock and Manure	38.2

**Some patients had several risk factors.*

In the present study, 15.7% of the patients had a history of infections in family members. The most common clinical symptoms of the patients included musculoskeletal and back pain (92.6%), and the least common clinical symptoms were adenopathy, splenomegaly, and hepatomegaly (1%) (Table 3). Regarding

the type of drug regimen, 71.6% of the patients had a two-drug regimen, and 23% had triple-drug therapy. According to the information in Table 3, the most commonly prescribed medications for the patients with brucellosis were rifampin (87.7%) and doxycycline (75.5%).

Table 3. Frequency Distribution of Clinical Symptoms of Brucellosis and Prescribed Medications (2014-2016)

Clinical Symptoms	N (%)	Prescribed Medications	N (%)
Fever	164 (80.4)	Tetracycline	12 (5.9)
Anorexia	112 (54.9)	Doxycycline	154 (75.5)
Weight Loss	71 (34.8)	Streptomycin	39 (19.1)
Musculoskeletal and Back Pain	189 (92.6)	Cotrimoxazole	41 (20.1)
Adenopathy, Splenomegaly and Hepatomegaly	2 (1)	Rifampin	179 (87.7)
Weakness and Fatigue	47 (23)	Gentamicin	12 (5.9)

**Some patients had several clinical symptoms.*

According to the results, 11 patients (4.5%) were hospitalized due to the complications caused by brucellosis, and 3.9% of the patients (n=8) experienced brucellosis complications.

Discussion

This was the first study on the incidence and epidemiology of brucellosis in Khomein city (Iran), and one of the studies that examined most of the aspects relating to the incidence and epidemiology of the disease. According to the findings, the IR values were higher than the ASR, which emphasized on the importance of using ASR as an indicator for the incidence of brucellosis.

The results of the present study indicated that the incidence of brucellosis was on a rising trend in 2015, while it reduced in 2016; the downward trend could be attributed to the proper implementation of the national program as a comprehensive system for the systematic education and promotion of health and vaccination of livestock in the region.

In the current research, mean incidence of brucellosis in the Khomeini city was 8.61 per 100,000 during three years. As mentioned earlier, this city is among highly polluted areas in Iran where the mean incidence of brucellosis has been estimated from 31 to 41 per 100,000 people [12]. This rate is higher than the incidence of brucellosis in France (0.3 per million), Saudi Arabia (12.5 per 100,000), and Mongolia (18.25 per 100,000) [16-18]. The incidence of the disease has been reported variably in different regions of Iran. For instance, the mean incidence of brucellosis has been reported to be 60 per 100,000 in Arak [19], 30.88 per 100,000 in the north and northwest of Iran [20], and 7 per 100 in Qom [21]. Furthermore, the mean annual incidence of brucellosis in Iran has been estimated at 24.43 per 100 [22], which is lower compared to the results of the present

study. Therefore, it could be concluded that Khomein is a highly polluted, high-risk area for brucellosis.

According to the present study, the prevalence of brucellosis was comparatively higher in men (7.62%) and rural residents (88.7%). Similarly, in a study by Farahani et al. [19] in Arak (Iran), 60% of the patients with brucellosis were male, and 72% were rural residents. In another study in Hamadan province (Iran), 62.8% of the brucellosis cases were male, and 7.81% were rural residents [23]. These findings are consistent with the results of the present study regarding gender distribution.

In another research performed in Kermanshah province (Iran), the incidence of brucellosis was reported to be comparatively higher in men (6.52%) and rural residents (6.87%), which is in line with our findings in terms of the distribution of the area of residence. Therefore, it could be inferred that brucellosis primarily affects rural men since they are usually in contact with livestock.

With respect to the occupational status of brucellosis patients, our findings indicated that the majority were farmers or ranchers (25.5%) and housewives, which is in congruence with the results obtained by Taheri Soodjani in Shahr-e-Kord (Iran) [14] Qom Rezai et al. [21], while inconsistent with the findings of Hashtarkhani et al. in Razavi Khorasan province (Iran) [25] and Hosseini et al. in Amol city (Iran). Based on the mentioned findings, it seems that occupation status is a risk factor for brucellosis. For instance, occupations involving livestock and animal husbandry could increase the risk of this infection, especially in rural communities where husbandry activities are often carried out by housewives.

In the present study, mean age of the patients was 40.9 years, and the majority of the subjects were within the age range of 20-29

and 59-50 years. This is consistent with the results obtained in Qom and Razavi Khorasan provinces in Iran [25]. The higher mean age of the patients with brucellosis in the present study compared to the findings in Hamadan province (Iran) [23] could be due to the high migration of the youth from rural areas, growth of the elderly population, and lack of animal husbandry activities. Moreover, it seems that the age pattern in brucellosis is changing from the youth to middle-aged individuals, which might render it a long-term disease in the future.

Investigation of the possible risk factors for brucellosis in the present study showed that 87.7% of the patients had a history of contact with livestock, especially through keeping livestock in their place of residence (74.5%). Furthermore, they consumed non-pasteurized dairy products (65.2%), especially milk (52%) and cheese (25.5%). In the studies by Ismail Zadeh et al. (2015) and Nematollahi et al. (2017), more than 85% of the subjects had a history of contact with livestock [23, 26], which is in line with the results of the present study.

In the studies by Pakzad [20] and Taheri [14], 78% and 85% of the patients had a history of non-pasteurized dairy consumption (especially milk and cheese), respectively. The reported rates in the mentioned studies are higher than our findings. With regard to the type of dairy products (milk and cream), the mentioned findings are inconsistent with the present study. This discrepancy could suggest the changes in the pattern of brucellosis transmission from food to work (contact with livestock) in Khomein city.

According to the current research, the most common clinical symptoms of brucellosis were musculoskeletal and back pain (92.6%) and fever (80.4%). In a similar study performed in Julfa (Iran) in 2015, musculoskeletal pain and fever were the

common symptoms of brucellosis [26]. In the other studies in this regard, fever, anorexia, and myalgia were the most common clinical manifestations of brucellosis in the patients, which is inconsistent with the results of the present study [25]. Therefore, it could be inferred that individuals who experience fever or musculoskeletal and back pain should refer to a laboratory for the necessary tests for brucellosis. In the current research, a remarkable point about laboratory tests was that the mean titres of Wright and 2ME tests were lower than the values reported in the other studies. In Khomein city, the titre of Wright's test was 1.160 (42.2%), and the titre of 2ME test was 1.80 (37.3%), which were higher than the previous studies in this regard [19, 21].

Findings of the current research demonstrated that the highest incidence of brucellosis was in summer (July), which is similar to the studies by Kasiri et al. in Azna [7] and Nematollahi in Hamadan (Iran) [23]; this consistency could be due to the similarity of the geographic climate. On the other hand, the highest incidence of brucellosis was reported to be in spring in Khorasan and Isfahan provinces (Iran) [9].

According to the results of the present study, rifampin (87.7%) and doxycycline (75.5%) were the main drug regimens in the patients with brucellosis, which are the medications prescribed for Maltese fever. This finding is in line with the results of the previous studies in this regard [7, 25].

Conclusion

Despite the gradual trend of reduction in brucellosis in 2016 compared to 2015, the mean incidence of brucellosis in Khomeini city was higher than the provincial and national average. As such, Khomein is considered to be an extremely high-risk region for the occurrence of brucellosis in Iran. In addition to stockbreeders, housewives

are also at a high risk of frequent contact with livestock. Moreover, after the consumption of milk, using local dairy cream was among the most important routes to develop brucellosis, especially in urban areas. According to our findings, the pattern of brucellosis transmission is changing from food to occupation and from youth to middle-aged individuals in terms of age. Nonetheless, brucellosis is likely to be known as an aging-associated disease in the future, and job (i.e., contact with livestock) and old age might be important factors in the transmission of brucellosis. Therefore, healthcare policymakers must pay special attention to this issue in order to plan and implement appropriate interventions through effective methods (e.g., Systematic Comprehensive Health Education and Promotion Model) and livestock vaccination and industrialization so as to decrease the incidence of brucellosis. Considering the conflicting results regarding the IR and ASR values in the current research

and previous studies, it is suggested that further investigation be conducted in the other regions in Iran, using ASR as an indicator to determine the incidence of brucellosis based on age differences for an accurate interpretation of the results.

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