ORIGINAL ARTICLE

Evaluating the Incidence and Recurrence of Brucellosis and Its Risk Factors in Fars Province from 2014 to 2018

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Abstract

Background: Brucellosis, a zoonotic disease, poses a significant health and economic challenge in many parts of the world, including Mediterranean and Middle Eastern countries. This study aimed to investigate the risk factors and recurrence of brucellosis, focusing on demographic variables such as age, gender, occupation, place of residence, and the spatiotemporal pattern of the population.

Methods: The study design was cross-sectional.The authors enrolled all Brucella cases registered in the infectious disease surveillance system of Fars province from 2014 to 2018 in the study. They performed a multivariate analysis of the disease risk factors using a Poisson regression model and a multivariate analysis of the risk factors associated with brucellosis recurrence using a logistic regression model.

Results: The incidence of brucellosis in Fars province exhibited a decreasing trend. The findings revealed that the sex ratio of patients who consumed unpasteurized dairy products, the mean age of patients per month, and the proportion of people living in rural areas relative to the total number of patients with brucellosis were significantly associated with the risk of brucellosis. Moreover, the probability of disease recurrence was higher in colder seasons compared to spring.

Conclusion: A higher ratio of lightweight livestock to heavyweight livestock was identified as a risk factor for brucellosis, indicating the more significant role of lightweight livestock in the incidence of brucellosis in Fars province. Therefore, controlling the disease in lightweight livestock is of paramount importance, and the vaccination of these livestock should be more strictly monitored and implemented.

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Keywords: Brucellosis, Fars province, Incidence, Recurrence, Risk factors

Introduction

Brucellosis is a significant health and economic concern in many parts of the world, including the Mediterranean and Middle Eastern regions. The World Health Organization (WHO) estimates that the global number of new brucellosis cases exceeds 500,000 annually.[1] While brucellosis is controlled in many developed countries, it remains a critical health surveillance issue in developing nations.[2]

Brucellosis in humans can occur through the consumption of raw, unpasteurized milk and its products, as well as the consumption of undercooked meat. Other transmission modes include bacterial

penetration through the skin, respiration, and exposure to contaminated airborne particles. Moreover, individuals in close contact with animals, such as veterinarians, medical laboratory staff, and animal slaughterhouse workers, can become infected through direct contact and airborne contaminants.[3] This medical condition has been detected worldwide, particularly in countries around the Mediterranean Sea (e.g., Southern Europe, North and East Africa), the Middle East, India, and Central Asia. Brucellosis has been endemic in most parts of Iran for years.[4]

Human and animal brucellosis has escalated in the Mediterranean, Middle East, West Asia, and Africa over the past twenty years.[5, 6] The recurrence of symptoms following treatment could be indicative of disease relapse. Bacteriological recurrence transpires within three to six months of continuous treatment, which may not be solely associated with antibiotic resistance.[7, 8] Furthermore, approximately 10% of patients with brucellosis experience disease relapse after antibiotic therapy. This could be attributed to the intracellular nature of the pathogen, lack of exposure to the prescribed antibiotics, and the host's antimicrobial defense mechanisms.[9]

Fars province, located in the south of Iran, has a moderate infection rate of brucellosis. According to the Infectious Diseases Management Center, Ministry of Health, Treatment, and Medical Education, the prevalence is between 11 and 20 per 100,000 population.[10] This province is home to 12% of the country's nomadic population, with four million livestock, including goats and sheep. The prevalence of active brucellosis in this province has been reported to be 10%, a figure significantly higher than that in the general population (e.g., 15.9 per 100,000).[11]

This study investigated the risk factors associated with brucellosis and its recurrence based on demographic variables such as age, gender, occupation, place of residence, spatiotemporal population patterns, and dietary habits related to dairy product consumption. The aim is to assist health policymakers in establishing effective prevention and control strategies to reduce the number of human brucellosis cases and its associated burden.

Methods

This study analyzed all brucellosis cases registered in the infectious disease surveillance system of Fars province from 2014 to 2018. The inclusion criterion for the study was a physician's confirmation of the disease using serological tests. The necessary data of the target population were extracted from the integrated health system (Sib) to calculate the incidence of brucellosis. The incidence rate of the disease was calculated by dividing the number of new cases by the total population. The recurrence rate of the disease was computed by dividing the number of recurrences by the total number of patients with brucellosis within the past 12 months.

Data analysis was conducted in three stages. Initially, the distribution of patients was described in terms of independent variables, and the incidence was determined at the level of these variables. Subsequently, the relationship between each independent and dependent variable was established. Finally, the relationship between the independent variables and the dependent variable, in the presence of other variables, was identified, culminating in the presentation of the final model.

In the first stage, the number of patients at each level of the designated variables was determined and tabulated to achieve the descriptive objectives (e.g., frequency of patients and incidence of brucellosis in terms of independent variables).

A univariate analysis was performed using the Poisson regression model in the second stage. Each variable's crude relative risk coefficient was extracted to determine the relationship between each variable and the outcome. The Poisson regression model determined the adjusted relative risk in two ways. Initially, all variables were entered into the model, and the value of the adjusted coefficients of each of these variables, along with their confidence interval, was determined. Subsequently, only the significant variables in the previous model (A) were entered into the model, and their relationship with disease incidence was evaluated to construct the final model. A logistic regression model was also employed to examine the relationship between the factors associated with disease recurrence.

Variables such as gender, consumption of unpasteurized dairy products, age group, and place of residence (e.g., urban, rural, or nomadic) were evaluated using a univariate chi-square test. Additionally, the relationship between seasons and disease risk in different seasons was assessed using the disease ratio test (Z test) and compared with a uniform distribution. Furthermore, the differences in disease incidence across the four seasons were investigated. Finally, a multivariate analysis of these factors was performed using the Poisson regression model.

Multivariate analysis of the risk factors for brucellosis recurrence was conducted using logistic regression analysis. All variables with a p-value less than 0.2 in the univariate analysis were included in the model. The backward LR method was utilized to select the variables in the model. The Variance Inflation Factor (VIF) was calculated to examine the collinearity between the variables. A VIF greater than ten was considered the threshold value. All analyses were performed using SPSS 26.0 software, and the significance level was set at 0.05.

Results

A total of 4025 cases of brucellosis were registered in the health surveillance system during the study period. Among these cases, 2320 (57.6%) were male. The mean age of the patients was 38.3±17.8 years. The highest prevalence of brucellosis was observed in Pasargad, Bavanat, Rostam, Khorrambid, and Farashband, with rates of 574, 570, 523, 465, and 446 per 100,000 population, respectively. Conversely, the lowest prevalence was reported in Mehr, Shiraz, Rostam, and Lamerd, with rates of 3, 18, 20, and 22 per 100,000 population, respectively (Table 1).

Figure 1 presents the decreasing trend of brucellosis incidence between 2014 and 2018.

Regarding age groups, the disease was most prevalent in the 25-44 age group, with 1604 cases accounting for 39.8% of the total. In terms of residence, the disease was most prevalent among individuals living in urban areas (n=1493), followed by those in rural areas (n=2084) and nomadic areas (n=448). The incidence of brucellosis was 110.4 per 100,000 in males, compared to 83.20 per 100,000 in females. The disease's highest and lowest incidence rates were observed in the 45-54 (136.8 per 100,000) and 15-24 (80.6 per 100,000) age groups, respectively. The highest incidence of brucellosis was found in the nomadic community, with a rate of 418.6 per 100,000 population. Moreover, the highest incidence of the disease was detected in spring, with a rate of 29.8 per 100,000 population, while the lowest rate was observed in winter, at 18.4 per 100,000 population. Furthermore, the disease incidence showed a descending trend across the seasons.

As shown in Table 2, factors such as sex ratio, consumption rate of unpasteurized dairy products, mean age, nomadic ratio, livestock-related occupations, and the ratio of light-weight livestock were significantly associated with brucellosis.

Table 1: The frequency and incidence of brucellosis based on demographic characteristics in Fars province from 2014 to 2018

Variables		No. of cases (n=4025)	Incidence (per 100,000)	P value
		n (%)		
Gender	Male	2320 (57)	110.40	<0.001
	Female	1705 (43)	83.20	
Living place	Urban	1493 (37)	50.81	<0.001
	Rural	2084 (52)	174.20	
	Nomadic	448 (11)	418.61	
Season	Spring	1240 (31)	29.82	<0.001
	Summer	1194 (29)	28.79	
	Fall	842 (21)	20.29	
	Winter	749 (19)	18.04	
Consumption of contaminated dairy products	Yes	496 (12)	17.07	<0.001
	No	3529 (88)	283.42	
Age group	0-14	408 (10)	43.17	<0.001
	15-24	478 (11)	80.61	
	25-44	1604 (39)	101.31	
	45-54	753 (18)	164.82	
	>55	782 (20)	136.61	

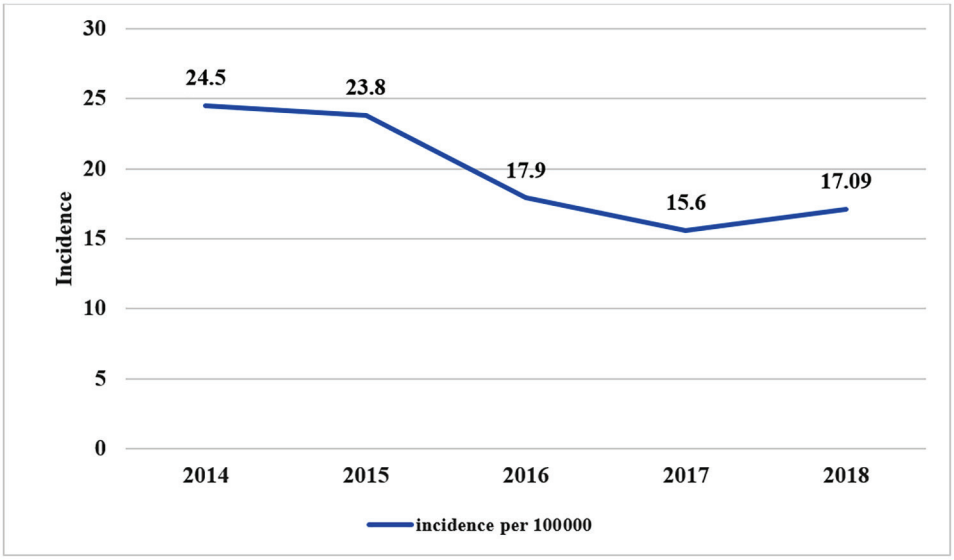

Figure 1: The trend of brucellosis in Fars province from 2014 to 2018

Table 2: Multivariate analysis of the risk factors associated with brucellosis using Poisson regression model

Variable	ARR*	95% confidence interval for RR**		P value
		Upper limit	Lower limit	
Unpasteurized dairy products consumption rate	4.10	3.22	5.20	<0.001
Sex ratio (males/total pop)	1.40	1.17	1.67	<0.001
Mean age	1.01	1.011	1.019	<0.001
Rural ratio	0.93	0.79	1.10	0.453
Nomadic ratio	1.84	1.41	2.39	<0.001
Light-weight livestock ratio	3.46	1.09	10.96	0.034

*Adjusted rate ratio; **Rate ratio

Table 3: Multivariate analysis of the risk factors associated with brucellosis recurrence using logistic regression analysis

Variables		Frequency	AOR*	95% confidence interval for OR**		P value
				Lower limit	Upper limit	
Consumption of contaminated dairy products	No (reference)	496	_			
	Yes	3529	0.68	0.48	0.98	0.039
Season	Spring (reference)	1240	_			
	Summer	1194	1.28	0.87	1.86	0.200
	Fall	842	1.61	1.09	2.38	0.016
	Winter	749	1.9	1.29	2.79	0.001
Age group	0-14 (reference)	408	_			
	15-24	478	1.17	0.55	2.49	0.672
	25-44	1604	2.17	1.18	4	0.012
	45-54	753	2.35	1.24	4.47	0.009
	>55	782	1.94	1.02	3.72	0.043

*Adjusted odds ratio; **Odds ratio

The multivariate logistic regression analysis (Table 3) revealed that individuals who consumed unpasteurized dairy products were 31% less likely to experience a disease recurrence than those who did not. Furthermore, the disease was more prevalent in the colder seasons than in spring. The odds of disease recurrence were higher in the 25-54 age group than in individuals under 14 years, and this difference was statistically significant.

Discussion

This study investigated the incidence of brucellosis and the risk factors associated with its incidence and recurrence in Fars province. The findings revealed a descending trend in the incidence of brucellosis over five years from 2014 to 2018. This trend aligns with the results of research conducted by Bagheri et al. in Iran in 2019.[12] The reduction was particularly significant in 2016, which may be attributed to implementing training interventions by the Communicable Disease Management Center in healthcare networks. Specifically, these interventions, conducted in the Systematic Comprehensive Health Education and Promotion (SHEP) model, discussed disease prevention methods. They were carried out by rural and urban health workers and health volunteers, reaching 100% of the rural and nomadic populations.

It should be noted that the Communicable Disease Management Center has classified provinces with a prevalence of 11-20 per 100,000 population as being in the middle range. Therefore, Fars province exhibited a middle-range incidence of brucellosis. This study also indicated that the incidence of brucellosis was significantly higher in males than in females. This finding was supported by a systematic review and meta-analysis conducted by Musazadeh et al. in 2016[13] and another study by Marvi et al. in Mazandaran province in 2018.[14] Similarly, a study conducted by Harriet N Muloki in northern Uganda in 2018 found a relationship between gender and the incidence of brucellosis.[15] One reason for the higher prevalence of brucellosis among males is that this condition is an occupational disease, and males are more frequently in contact with livestock. Furthermore, HAAL-Shamahy et al.[16] (2000), Shama Cash-Goldwasser et al.,[17] Musazadeh et al.,[13] and Behnam Honarvar et al.[18] concluded that the consumption of unpasteurized dairy products was a risk factor for brucellosis, which aligns with the results of the present investigation.

The disease incidence was 50.8, 174.2, and 418.6 per 100,000 population in urban, rural, and nomadic areas. Consequently, the incidence of the disease was higher in nomadic communities. This could be attributed to the nomads' unique lifestyle, close contact with livestock, and consuming contaminated dairy products. These results agreed with those of a cross-sectional study by Honarvar et al. among the nomads of Fars province in 2017.[18]

In the present study, the incidence of the disease was 29.8 per 100,000 in the spring. This can be attributed to the fact that spring is the breeding season for

livestock. During this time, consuming contaminated dairy products, especially colostrum, cottage cheese, and traditional cheese that do not undergo proper heat treatment during the preparation process, as well as contact with the placenta and assisting at calving, is considerably increased. These findings aligned with a systematic meta-analysis performed by Musazadeh et al.[13] and a cross-sectional study conducted by Pakzad et al.[19]

In the current study, the disease incidence was diversely distributed across age groups, with the highest reported in the 45-54 age group (164.8 per 100,000 population). Aloufi et al. (2016) conducted a study in Saudi Arabia and found that most patients were in the 15-44 age group.[20] Similarly, Hamzavi et al. (1990) conducted a study in Kermanshah province and reported that half of the patients were under the age of 30 years.[21] In contrast, Shahrzad Nematollahi et al. revealed the highest incidence of brucellosis among individuals aged 50 years and above.[22] Meltem Isigoz Tabaskan also showed the highest prevalence of brucellosis in the 41-50 age group (39%). One possible explanation for the higher incidence of the disease in older ages could be their lower awareness and, consequently, a higher likelihood of ignoring health protocols.

The results of the present study indicated that the recurrence rate of brucellosis was 5.7%. Seyed Mohammad Alavi et al. (2009) conducted a study in Ahvaz and reported the recurrence rate of the disease to be 18.3%.[23] Nematollahi et al. also conducted research in Hamadan province and found the recurrence rate of brucellosis to be 6.4.[22] The lower recurrence rate in Fars province could be attributed to more efficient control and treatment of patients identified at an earlier stage and proper adherence to long-term drug regimens, which can sometimes last as long as two months.

One of the present study's strengths was utilizing five years of provincial data. Additionally, the study employed a population-based design and examined 4025 cases of brucellosis, whereas previous studies were case-control, hospital-based, or seroepidemiological with smaller sample sizes.

However, this study had several limitations. Its retrospective design and reliance on patients' medical records data were among these. The information about the medications used by the patients and their usage patterns, which play a crucial role in the recurrence of brucellosis, was incompletely recorded, rendering it unsuitable for data analysis. Furthermore, none of Fars province's veterinary organizations and agricultural institutes maintained livestock vaccination coverage records during the study years. Consequently, the impact of this significant variable on the incidence of brucellosis in different cities could not be investigated. Another limitation was the inaccuracy of the statistics regarding the number of lightweight livestock in each city, as traditional and semi-industrial livestock houses were included. In contrast, those keeping homemade livestock were excluded.

Conclusion

The present study's findings demonstrated that gender, age, consumption of traditional and unpasteurized dairy products, and a nomadic lifestyle were risk factors for brucellosis. An elevated ratio of lightweight livestock (e.g., goats and sheep) to heavyweight livestock (e.g., cattle, buffaloes, and camels) was also identified as a risk factor for brucellosis in Fars province. Therefore, responsible organizations should seriously consider disease control in livestock and proper vaccination.

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Ethics Approval and Consent to Participate

The approval number for the ethics of the present study was "IR.SUMS.REC.1398.401.

Availability of Data and Material

The data supporting this study's findings are available from the corresponding author, [HGH], upon reasonable request.

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Authors' Contribution

HGH (Principal Investigator) led the design and conduct of the study throughout and drafted the manuscript. MHB coordinated the study and contributed to drafting the manuscript. MS, ME, ARR, and MV contributed to the design and analysis of the study. All authors read and approved the final version of the manuscript. Additionally, all authors have approved this paper's contents and agreed to the Health Research Policy and

Systems submission policies.

Conflict of Interest: None declared.

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