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Original Article

Spatiotemporal analysis of brucellosis cases in Golestan province from 2015 to 2017 years using Geographic Information System

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Summary

Brucellosis is one of the most prevalent bacterial zoonotic diseases considered as a public health problem in Golestan province (north-east of Iran), but its spatial pattern remains unclear. Hence we evaluated the spatial analysis of brucellosis disease in Golestan province during 2015-2017. In this study, we explored the Spatial and Spatiotemporal clusters by using scan-statistic to consider influencing factors. In addition, logistic regression and Pearson's chi-square tests were used to analyze the clusters' zones and compare them with others. We used GIS to determine unites' (Golestan cities) coordinate centers and visualize the location of the clusters. Results revealed that the geographical distribution of brucellosis in Golestan province was affected by several spatial and spatiotemporal clusters. Constituent units of both spatial and spatiotemporal clusters were the same, but the identified time period of spatiotemporal clusters was from January 2015 to June 2016. The main influencing factors were in contact with livestock and dairy hygiene. This study can assist health authorities to plan more effectively to control diseases by highlighting the high-risk areas and behaviors.

Keywords: Brucellosis; Spatial analysis; Golestan province; Geographic Information System

Introduction

Brucellosis is a prevalent bacterial zoonotic disease, which is an important health burden causing an abortion in animals as well as a fetal multi-system sickness in human beings. WHO reports that there are more than 500,000 cases of brucellosis worldwide diagnosed annually, especially in the developing countries, while four cases remain undetected per a diagnosed case (Zeinalian Dastjerdi et al., 2012). Common symptoms of brucellosis are fever, night sweating with a peculiar odor, chilling, weakness and malaise, arthralgia, constipation, sexual impotence, being nervous, insomnia, anorexia, headache, and depression (Seleem et al., 2010). Simple infections of brucellosis without complications can usually be treated successfully with antibiotics, which the therapy often takes several weeks to months, although relapsing is common. (Von Bargen et al., 2012)

Despite a well-established Primary health care system (PHC), Iran is one of the top five countries with a high incidence rate of brucellosis disease, especially in rural areas (Haghdoost et al., 2007). Socio-economic and environmental conditions, as well as brucellosis distribution in a community, can influence the incidence rate strongly (Mirnejad et al., 2017). Most parts of Iran are endemic for the disease, particularly the areas where humans live in close contact with livestock (Sofian et al., 2008). The prevalence of human brucellosis depends on factors such as socio-economic situation, environmental hygiene, dietary habits, husbandry practices, methods of processing milk, and dairy products (Gwida et al., 2010).

There is a considerable variation in the prevalence of brucellosis in different parts of Iran, and the incidence rate differs from 98 to 130 per 100,000 of the total population. The lowest and highest incidence rates of brucellosis infection is in the south and west parts of Iran respectively (HR et al., 2010)

Previous studies showed that the prevalence of brucellosis was higher during the first half of the year, which was the livestock calving season and it decreases in the second half of the year. Thus, during spring and summer, consuming contaminated dairy products, and direct contact of ranchers' skin whit aborted fetuses increase the rate of brucellosis (Moosazadeh et al., 2016).

Numerous studies considered epidemiological aspects of brucellosis in different provinces of Iran. A cross-sectional study done in the northeast of Iran showed that the prevalence rate of brucellosis in human beings was 31.9 in 100,000 people during 2008-2009 (HR et al., 2010). In the study of Esmailnasab et al. on epidemiologic changes of malt fever in Kurdistan province, it was revealed that the disease had a downward trend in 2006 in comparison with 2004 and 2005 (Esmaeilnasab et al., 2007). Another cross-sectional study done in all provinces of Iran during 2009 to 2011showed that majority of the events belong to Markazi province (8.9% cumulative incidence) followed by Lorestan (7.2% cumulative incidence) and Kermanshah provinces (6.8% cumulative incidence) (Mollalo et al., 2014).

A study carried out in Golestan province showed that the incidence rate of the disease in the province was 47,67,33,29 and 24 per 100000 of the population from 2000 to 2004, respectively. After classification of the cases according to their residency area, two high prevalent regions were found, which were in the eastern part of the province (Gonbad, Minoodasht, Kalaleh) and western part

(Kordkooy, Bandargaz) (Rahnama et al., 2006).

Brucellosis is debilitating in its acute form and, if be untreated, may become chronic with acute recurrent episodes and debilitating complications (Bokaie et al., 2008). Like other parts of Iran, the disease is endemic in Golestan provine because domestic farm animals, especially sheep and goats are abundant, and the use of dairy products is common. Golestan province is considered as a free trade zone, agricultural and animal husbandry center in Iran due to the special geographical location. So, a considerable number of people travel to this province (Sofizadeh et al., 2014). According to Moore and Carpenter, three major influencing factors in every epidemiological study are person, place and time (Mollalo et al., 2015), GIS(geographical information systems) can be used to assess the occurrence of the disease in the same way as other studies used it in Iran and other countries to determine the disease distribution pattern (Kulldorff et al., 2006).

The main aim of this study was to evaluate the incidence rate of brucellosis by the GIS program in Golestan province during 2015-2017.

Materials and Methods

Study area

Golestan is located in the north-east of Iran and lain within the 36°30′–38°8′ N and 53°57′–56°22′ E with 20893 square kilometers area. It consists of 14 major cities and 1069 villages with over 1800000 population in 2016. The region has a variety of climates and has a wide range of altitudes (up to 500 and even 3000 m above the sea level). The climate of Golestan varies from arid to subtropical with average rainfall between 250-700 mm/year and the mean temperature of 20 ºC. Health facilities in Golestan province are mostly governmental, and health workers try to find cases of diseases such as brucellosis actively. They record and report suspected disease cases to the center of the province (Gorgan) every month. Physicians visit all of the suspected cases, and final diagnosis will be made based on serologic laboratory testing.

Study design, data collection

In this cross-sectional study, brucellosis data was obtained from district official health centers, and it was classified by variables such as city, age, sex, contact with livestock, consumption of dairy products, positive family history, complications, and hospitalization of the cases. In addition, some of the data was downloaded from the Census population data of the Iranian statistic center (Statistical Centre of Iran, 2018).

Table 1. Frequency distribution of patients based on demographic information from 2015 to 2018 in Golestan Province.

Variables		Frequency	Percent
Diagnostic year	2015	507	38.4
	2016	447	33.9
	2017	361	27.4
Gender	Male	877	66.5
	Female	422	33.5
Contact with livestock	Yes	1079	85.7
	No	180	14.3
Non-pasteurized dairy consumption	Yes	1112	89.5
	No	130	10.5
Positive family history	Yes	158	13.3
	No	1029	86.7
Complication	Yes	37	4.5
	No	794	95.5

	Yes	72	7.9
Hospitalization	No	841	92.1

Spatial analysis approach

In this cross-sectional study, we used the space-time scan statistic to identify the probable clusters of brucellosis in Golestan province. Therefore, we used the SaT Scan software version 9.6 (Pakzad et al., 2016). We also used the Geographic Information System (GIS) to assign the coordinate center of units (Golestan cities) and to depict the SaT Scan output results. Chi-square test and logistic regression analysis were used subsequently to compare the cluster and non-cluster areas. We considered $P < 0.05$ as the significant level for all of the analyses.

Table 2. Significant spatial-temporal clusters of brucellosis with discrete Poisson distribution spatial clusters

Cluster profile	Number of city	Radius (km)	Time frame	population	Number of cases	Expected cases	RR	Log LR	P-value
Cluster 1	Minodasht, AzadShahr, Galikesh, Ramiyan	37.91	2015/1/1 to 2016/5/31	804211	192	93.84	2.22	43.33	0.000
Cluster 2	BandarTorkaman, Gomishan, Kordkuy, BandarQaz	27.5	2015/1/1 to 2016/5/31	377364	124	52.32	2.51	37.39	0.000

Results

Descriptive analysis

Annual differences in the incidence rate of the disease were ranged from 507 cases in 2015 to 361 cases in 2017 from the total number of 1318 brucellosis cases reported in Golestan province from brucellosis surveillance system data. Fourteen cities that had about 2 million residents were totally affected by brucellosis. Maraveh and Gorgan had the highest and the lowest incidence rate of the disease, respectively. The mean age of the patients was 35.48 ± 1.66 years old. From 1318 cases, 66.54% were male, and 33.46% were female. Detailed demographic information is followed in Table 1. The hot-spot analysis showed that high-risk areas were concentrated in the west and south-east of Golestan. Meanwhile, the distribution pattern differed during the study period: the number of high-risk areas in the north-east decreased, and the counties located in the north-west and west of the province showed an increase in the risk.

Spatiotemporal clusters

Spatial-temporal clusters analysis of brucellosis data with discrete Poisson distribution detected two clusters in the study areas. The first cluster included Minoodasht, Azadshahr, Galikesh, and Ramiyan cities, and the second cluster included the cities of Turkman, Gomishan, Bandar Qaz, and Kurdkoy. Detailed information of clusters is shown in Table 2.

Purely Spatial clusters

Spatial clusters analysis of brucellosis data with discrete Poisson distribution also

distinguished two clusters that their detailed information is shown in Table 3. The first cluster included Minoodasht, Azadshahr, Galikesh, and Ramiyan cities, and the second cluster included the cities of Turkman, Gomishan, Bandar Qaz, and Kurdkoy (Figure 1). The relationship between independent variables and the formation of brucellosis disease clusters was assessed using Univariate analysis. It was shown that gender, contact with livestock, non-pasteurized dairy consumption, presence of complications and hospitalization, were more important variables in the disease transmission (Table 4). Clusters and non-clusters differ in their contact with Livestock, non-pasteurized dairy consumption, and hospitalization. These results partially approved the potential differences between the cluster and non-cluster areas. The statistically significant associations were confirmed in the regression analysis, and variables of age and sex remained significant in the model (Table 5).

Discussion

Brucellosis is one of the major infectious diseases in Iran, especially in Golestan province, and our study represents the need to provide appropriate interventions in different parts of Golestan province to reduce the incidence rate of the disease. We observed two primary clusters in the study areas, which represented 24% of cases in themselves with the centrality of Minodasht and Torkaman.

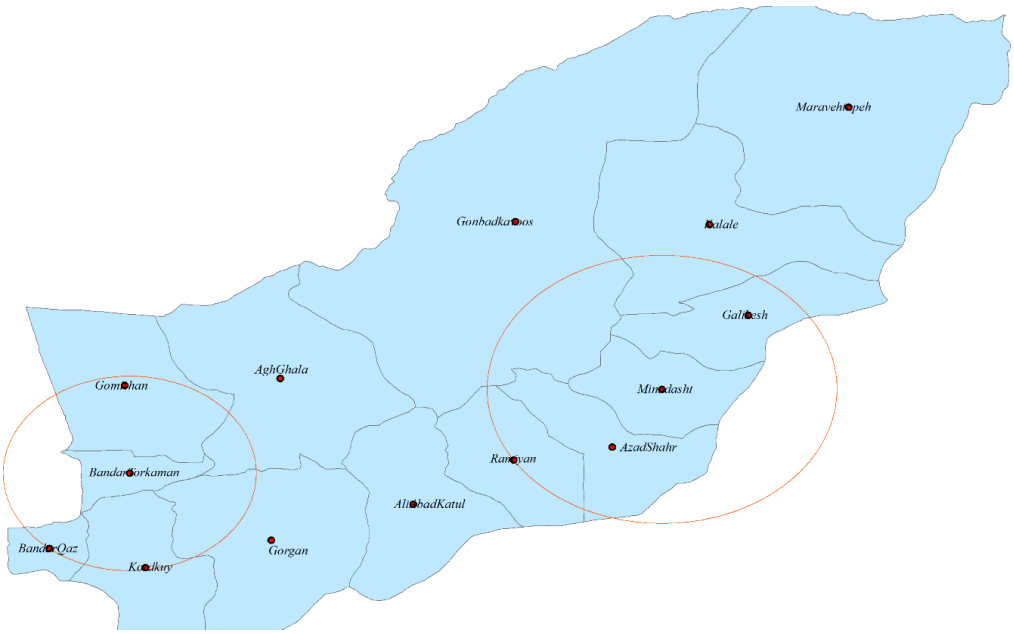

Fig. 1. Geographical locations of brucellosis clusters in Golestan Province.

In this study, the results showed that both genders were susceptible to the disease. Although, in most of the studies, the highest incidence rate of brucellosis was seen in males, which may be the result of more exposure to infected livestock in their occupation (Salari et al., 2003; Zeinalian Dastjerdi et al., 2012). The

difference of the results of this study may be due to the special characteristics of tribes and their common culture in Golestan province, which results in working women besides men, particularly in the rural areas.

In most parts of the world, brucellosis can be recognized as an occupational disease, and despite the prevalence of brucellosis is often higher in younger people (Esmaeilnasab et al., 2007), in our study, it was detected in all ages. The reason for the difference in age distribution in this study with other studies may be cultural characteristics and different ways of ranching, such as keeping livestock in the yards, which leads to whole family exposure to animals and their excreta. In the study of Zelinalian Datjerdiet et al mean age of cases was 31.3, and the disease was more prevalent in young people due to more contact with infected animals and unpasteurized dairy consumption, but there was no significant relationship between any age groups and incidence rates of the disease. Zeinalian Dastjerdi et al., 2012).

Table 3. Significant spatial clusters of brucellosis with a discrete Poisson distribution

Cluster profile	Number of cities	Radius (km)	population	Number of cases	Expected cases	RR	Log LR	P-value
Cluster 1	Minodasht, AzadShahr, Galikesh, Ramiyan	37.91	804211	392	203.26	2.32	85.68	0.000
Cluster 2	BandarTorkaman, Gomishan, Kordkuy, BandarQaz	27.5	377364	222	95.38	2.6	67.72	0.000

Spring is the season of breeding in livestock, especially small ones such as sheep and goats. As these animals are the main source of brucellosis, the disease is considerably more prevalent in the spring in comparison to other seasons.

In the investigation of Mollalo and Moosazadeh (Mollalo et al., 2014; Moosazadeh et al., 2016), there was a significant association between increasing of brucellosis and temperature but in our study incidence rate of brucellosis did not follow a clear seasonal pattern which might be due to the moderate climate and monotonous diary consumption all over the year in the study region.

Brucellosis was mostly transmitted to humans by direct contact with infected livestock, using unpasteurized milk or dairy products, inhaling aerosols, and entering through skin abrasions and cuts (Obradović and Velić, 2010).

The possibility of transmission of the disease is higher after delivery, whether full-term or aborted. An outbreak happened in Dallas in 2016 that 25 brucellosis cases were diagnosed, and all of them were caused by unpasteurized dairy products particularly cheese (Ward et al., 2017).

The case-control study of Sofian et al. showed that consumption of unpasteurized-diary-products was an important risk factor for brucellosis, (Sofian et al., 2008).

In our study, the main way of transmission of the disease was also contact with infected animals and using unpasteurized dairy products. Therefore, by the results, it is

expected to prevent the disease in the province considerably by focusing on these two ways.

Table 4. Descriptive and analytic characteristic of purely spatial clustered and non- clustered *Brucella*

	Clustered	**Non-clustered**	***P*-value**	**Unadjusted OR(95%CI)**	***P*-value**	**Adjusted OR(95%CI)**	***P*-value**
Gender			0.37	0.99		0.81 (0.58 - 1.13)	0.395
Female	205 (33.4)	236 (33.5)					
Male	409 (66.6)	468 (66.5)					
C.W.L[a]			0.028	1.43(1.04 – 1.96)		1.704 (1.11 - 2.62)	0.015
No	101 (16.5)	79 (12.2)					
Yes	510 (83.5)	569 (87.8)					
N.P.D.C[b]			0.046	1.45 (1.01 – 2.09)		1.89 (1.2 - 2.99)	0.006
No	74 (12.3)	56 (8.8)					
Yes	530 (87.7)	582 (91.2)					
Complication			0.05	1.91 (0.97 – 3.77)		1.677(0.78 – 3.59)	0.184
No	427 (96.8)	367 (94.1)					
Yes	14 (3.2)	23 (5.9)					
Ho[c]			0.005	0.49 (0.29 – 0.82)		0.411(0.23 – 0.75)	0.004
No	417 (89.7)	424 (94.6)					
Yes	48(10.3)	24 (5.4)					

[a] Contact with Livestock, [b] Non-pasteurized dairy consumption, [c] Hospitalization

Other studies have previously reported cluster behavior of brucellosis (Abdullayev et al., 2012; Mollalo et al., 2014). In our study, in the cluster and non-cluster areas, contact with livestock, non-posturized dairy consumption, and hospitalization had a different pattern, which was in agreement with other studies (Abdullayev et al., 2012; Mollalo et al., 2014). It was observed that exposure to unpasteurized dairy products was significantly different between the cluster and non-cluster areas.

Therefore, while investigating the cause of this difference is necessary, prevention programs should be based on this finding.
Hospitalization rates were two times more in cluster areas than in non-cluster ones which might be due to difference in brucellosis species in these areas although it needs to be more studied.

Table 5. Descriptive and analytic characteristic of spatiotemporal clustered and non- clustered *Brucella*

	Clustered	Non-clustered	*P*-value	Unadjusted OR(95%CI)	*P*-value	Adjusted OR(95%CI)	*P*-value
Gender			0.37	1.05 (0.81 – 1.38)	0.69	1.18 (0.83-1.66)	0.352
Female	103 (23.3)	339 (76.7)					
Male	213(24.3)	664 (75.7)					
C.W.L[a]				0.842 (0.59 – 1.2)	0.342	0.952 (0.61- 1.48)	0.83
No	50	130					
Yes	264						
N.P.D.C[b]			0.002	0.55 (0.38 – 0.82)	0.003	0.48 (0.31 – 0.76)	0.002
No	47 (36.2)	83 (63.8)					
Yes	266 (23.9)	846 (76.1)					
Complication			0.001	0.144 (0.03 – 0.60)	0.008	0.141 (0.03- 0.61)	0.008
No	226 (28.5)	568 (71.5)					
Yes	2 (5.4)	35 (94.6)					
Session			0.0001	1.2 (1.08 – 1.37)	0.001	1.48 (1.3 – 1.7)	0.0001
Spring	91(22.8)	309 (77.2)					
Summer	76 (17.8)	351 (82.2)					
Falls	80 (29)	196 (71)					
winter	69 (32.1)	146 (67.9)					

[a] Contact with Livestock, [b] Non-pasteurized dairy consumption

Physicians in both endemic and non-endemic areas must become aware and consider brucellosis in their differential diagnosis of febrile diseases with peculiar musculoskeletal or other focal findings (Franco et al., 2007). In contrast with our study, in a study conducted in Spain, 59.9% of patients were misdiagnosed, and a lot of them underwent surgery (Zheng et al., 2018). The relatively high frequency of hospital care in the Golestan province seen in the study may probably be due to meticulous physical

examination and rapid laboratory evaluation, which would assist the diagnosis.

The diversity of variables that can affect the assessment of the incidence rate of brucellosis such as the climate of the region, type of animals, which are breeded, people who use unpasteurized-diary-products, and do not refer to health centers or hospitals and so on were the limitations of our study.

Based on our findings, it is necessary to have continuous national surveillance programs to control and prevent brucellosis in Golestan and other endemic provinces. Meanwhile, diagnosing infected animals as soon as possible by periodic examination and application of tests, paying more attention to slaughter policies, using vaccination programs, and finally advice all to use pasteurized dairy products are essential to restrict the spread of brucellosis.

Conclusion

Brucellosis may lead to severe morbidity, and it has been an important health concern in the north-east of Iran (Golestan province). As there is no recommended treatment for complicated forms yet, it is necessary to plan multicenter studies with more cases to reach better therapeutic choices, especially in these types.

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