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Spatiotemporal analysis of brucellosis incidence in Iran from 2011 to 2014 using GIS

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ABSTRACT

Objective: To investigate the distribution and trends associated with brucellosis incidence rates in Iran from 2011 to 2014.
Methods: The reported incidence rates of brucellosis for the years 2011–2014 were collected and entered into GIS 10.1. The Cochran–Armitage test for linear trends, choropleth maps, hot-spot analysis, and high–low clustering analysis were used to investigate patterns of the disease over the study period and by season, and to identify high-risk areas and any clustering of the disease. The significance level was set at $p < 0.05$.
Results: A total of 68 493 cases of brucellosis were reported during the study period, giving an average brucellosis incidence rate for this period of 38.67/100 000. In 2011, the highest rate of brucellosis was observed in Koohrang County of Chaharmahal-Bakhtiari Province, with 317/100 000. In the subsequent years, 2012–2014, Charuymaq County of East-Azerbaijan Province had incidence rates of 384, 534, and 583/100 000, respectively. However, the incidence rate of the disease did not follow a linear trend ($p < 0.001$). The maximum and minimum incidence rates of the disease occurred in mid-summer and mid-winter, respectively. The results of the hot-spot analysis showed that the distribution of the disease was highest in the mountainous areas of Iran, particularly along the Zagros mountain range and in most cities near the Zagros Mountains ($p < 0.01$). In addition, the cluster analysis showed a clustering pattern in these high incidence areas ($p < 0.01$).
Conclusions: 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. The incidence of this disease also increased during the summer. It is important to take these patterns into account when allocating resources to combat this disease and to ensure that health programs and other interventions focus on the areas of greatest need.

Introduction

Brucellosis, classified as a zoonotic disease, is caused by Gram-negative bacteria of the genus *Brucella* (Earhart et al., 2009; Kamal et al., 2009). It is the most prevalent zoonotic disease and has led to more than 500 million cases worldwide; with more than 500 000 new cases annually (Pappas et al., 2006).

The disease is strongly influenced by economic, social, and environmental conditions (Dean et al., 2012) and the degree of community involvement (Kamal et al., 2009; Kirk et al., 2015), and it places a heavy financial and health burden on the health systems

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of many countries (Pappas et al., 2006; Dean et al., 2012; Hotez et al., 2012; Salari et al., 2003). Furthermore, brucellosis is the most commonly neglected bacterial disease in the world (Hotez et al., 2012).

Due to changes in lifestyle and the environment, the ecology of brucellosis is undergoing a great deal of change (Pappas, 2010), which has led to an uneven distribution of the disease across the world. In comparison to the countries of Europe and North America and other developed regions of the world, the main burden of the disease lies in the countries of the Middle-East, particularly in Syria, Iraq, Egypt, Turkey, and Iran (Pappas et al., 2006; Dean et al., 2012; Sofian et al., 2008).

In addition to inter-country differences in the occurrence of the disease, there are also substantial differences within countries. For example, incidence rates within Iraq and Egypt have been found to differ by 4–5 times depending on the region. This highlights the influence that geographical, environmental, socio-economic, and lifestyle factors have on the occurrence of the disease (Hotez et al., 2012).

In Iran, as in most countries of the Middle-East, brucellosis is an endemic disease (Pappas et al., 2006). Cases of the disease have been reported in all provinces of the country. However, the distribution of the disease across the country is not even, and reports have indicated that the incidence of the disease is higher in the western and northwestern provinces than elsewhere (Zeinali et al., 2009). According to the most recent data, the regions in Iran with the highest incidence of the disease are the provinces of Lorestan, Markazi, East-Azerbaijan, and Kermanshah, with rates ranging from 31 to 41/100 000 (Zeinali et al., 2009). Furthermore, the incidence of the disease has demonstrated a clear seasonal pattern, with decreased dairy and farm products during certain periods, which thereby places an increased economic burden on the affected residents (Awad, 1998; Eini et al., 2012; Mostafavi and Asmand, 2012).

It appears that location and time are two important factors in the distribution of brucellosis. One approach to the assessment of the impact of time and location on the occurrence of a phenomenon is the use of geographical information systems (GIS). A number of studies have used GIS to determine the distribution patterns of diseases in Iran and in other parts of the world (Mirzazadeh et al., 2009; Mostafavi et al., 2013; Pakzad et al., 2015a; Mahdavifar et al., 2015; Pakzad et al., 2015c; Pakzad et al., 2015b). However, the spatiotemporal distribution of brucellosis has not yet been investigated using this approach and there are considerable gaps in knowledge regarding its distribution. The aims of this study were: (1) to examine the spatial distribution of brucellosis in Iran; (2) to identify the high risk areas across Iran; and (3) to assess the time trends for the occurrence of brucellosis, if any. It was anticipated that the results would contribute to appropriate decision-making and accurate targeting of health interventions.

Materials and methods

Study area

Iran is a country in the Middle-East covering an area of 1 648 195 square kilometers. It is the 18th largest country in the world, with a population of over 80 million in 2016. The country has a variety of environmental conditions in terms of geography and topographic diversity, and has a wide range of altitudes (up to 5671 m above sea level). The climate of Iran varies from arid to subtropical, with a mean rainfall ranging between 100 and 2000 mm/year; the temperature ranges from −10 to 50 °C. Iran is bordered by Armenia, Azerbaijan, and Turkmenistan to the north (as well as by Russia and Kazakhstan via a water border in the Caspian Sea); Afghanistan and Pakistan to the east; the Persian Gulf and Gulf of Oman to the south; Iraq to the west; and Turkey to the north-west. The country is currently divided into 31 provinces and 388 townships (Holakouie-Naieni et al., 2017).

Study design, data collection, and 'join tables' to GIS

The present study was an ecological study performed in Iran. The reported incidence rates of brucellosis were collected at the township level, from the beginning of 2011 to the end of 2014. After cleaning and correcting errors, the data were entered into Excel datasheets. In situations where the only available information was the number of cases reported, the incidence rate was calculated (Equation (1)) by defining the population at risk as the total population of the township reported by the National Bureau of Statistics. The most recently updated electronic map of Iran and its townships was used, and the map was linked to Excel with the join comment.

$$\textit{Incidence rate of brucellosis} = \frac{\textit{Number of reported cases}}{\textit{Total Population at Risk}}\,100\,000 \tag{1}$$

Time trend reviews

For the assessment of trends in the disease incidence rate, the Cochran–Armitage test was used to identify linear trends during the study period. This test was used to determine whether there were any significant changes in the disease incidence rate over the study period (Nam, 1987).

GIS analysis

Choropleth map

A choropleth map, which uses a color range to show changes in the layers of polygons, was produced at the township level.

Hot-spot analysis (analytical map)

Identifying disease hot-spots was done using the Getis-OrdGi* statistic. The hot-spot analysis tool was used to calculate the Getis-OrdGi* statistic (Equation (2)) for each township in the dataset. The resultant Gi* score showed townships with either high or low incidences clustered spatially. This tool works by looking at each township within the context of neighboring townships. A township with a high incidence rate of brucellosis can be a statistically significant hot-spot providing that it has a high incidence rate of brucellosis and is surrounded by other townships that have high incidence rates.

$$Gi^* = \frac{\sum_{j=1}^{n}\omega_{i,j}x_j - \bar{X}\sum_{j=1}^{n}\omega_{i,j}}{S\sqrt{\frac{\left[n\sum_{j=1}^{n}\omega_{i,j}^2 - \left(\sum_{j=1}^{n}\omega_{i,j}\right)^2\right]}{n-1}}} \tag{2}$$

Equation (2): Getis-Ord Gi* (Gi* Statistics) - where Xj is the Incidence of brucellosis for Township j, wij is the spatial weight between Townships i and j, n is equal to the total number of Townships.

The local sum for a township, and its neighbors, is compared proportionally to the sum of all of the townships. When the local sum is considerably different to that expected, and that difference is too large to be the result of random chance, a statistically significant Gi* score results. Conversely, a cold-spot is a township that has a lower incidence rate and is surrounded by other townships with low incidence rates of brucellosis. Townships that were higher or lower than the national average (standard deviation 1.96) were considered hot-spots or cold-spots, as they were significant at the 0.05% level (Asgari, 2011).

For the hot-spot analysis, the spatial weight was calculated using the fixed distance band method. With this method, each township is analyzed within the context of the neighboring townships. Neighboring townships inside the specified critical distance receive a weighting of 1 and exert an influence on the calculations for the target township. Neighboring townships outside the critical distance receive a weighting of 0 and have no influence on a target township's computations. Also, in order to determine the critical distance, the Euclidean distance method was used, which is the straight distance between two polygon centers. In other words, it is the shortest distance between two polygons centers. The center of the polygons was determined using the centroid method and standardization was not used during weighting.

High–low clustering analysis

High–low clustering analysis was used to identify the concentration of high or low incidence rates of brucellosis for a given study area. General statistics (G statistics) were used for this purpose. This method was developed by Getis and Ord and is capable of measuring how the high and low incidence rate areas are distributed (Holakouie-Naieni et al., 2017). A positive or negative *Z*-score for G(*d*) indicates spatial clustering of a high or low incidence rate, respectively (Equation (3)) (Asgari, 2011).

$$G = \frac{\sum_{i=1}^{N}\sum_{j=1}^{N}\omega_{ij}x_i x_j}{\sum_{i=1}^{N}\sum_{j=1}^{N} xixj}, \forall j \neq i \quad (3)$$

Equation (3): G statistics where x_i and x_j, respectively, are the Incidence of brucellosis in the i^{th} and j^{th} Townships; Wij is the spatial weight between the Township i and j; N is the total Incidence of brucellosis; and S_0 is the aggregate of all spatial weights.

Ethical approval

This study was approved by the Ethics Committee of Tehran University of Medical Sciences.

Results

Overall findings and time trends

A total of 68 493 cases of brucellosis were reported during the study period in Iran, giving an average brucellosis incidence rate for this period of 38.67/100 000. The results also demonstrated a pronounced seasonal pattern, with an increase in the number of cases in spring that continued well into mid-summer. Following this peak in mid-summer, the number of cases decreased to the lowest level in early winter (Figure 1). The results of the Cochran–Armitage test showed that the disease incidence rate did not follow a linear trend ($p < 0.001$).

Spatial modeling

The analyses showed that in 2011, the highest incidence rate of brucellosis was observed in Cohrang County of Chaharmahal-Bakhtiari Province, with 317/100 000. In the subsequent years (i.e., 2012, 2013, and 2014), Charuymaq County of East-Azerbaijan Province had rates of 384, 534, and 583/100 000, respectively. Descriptive maps showed that the disease incidence rate was highest in the north-east, west, and north-west of the country; thus, most of the counties in this region are considered to have a high incidence rate of the disease. However, the number of cases increased while the incidence rate of the disease decreased over the study period. Furthermore, during the study period the disease became more concentered in the west and north-west (Figure 2).

The hot-spot analysis showed that high-risk areas were concentrated in the north-west and north-east of Iran. However, the distribution pattern differed across 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 country showed an increase in risk. Also, most low risk areas were in the coastal cities of the Caspian Sea and the Persian Gulf (Figure 3).

Clustering analysis

High–low clustering analysis demonstrated that the disease had a clustering distribution and that this clustering occurred in areas with high incidence rates (Figure 4).

Discussion

Brucellosis is one of the most prevalent zoonotic diseases in Iran. Despite the health measures taken during recent years, the rate of disease is still high, with 68 493 cases of brucellosis being reported in Iran during the study period. However, it should be noted that because of variations in the level of clinical diagnosis as a result of not visiting a doctor (for mild forms of the disease), incorrect or slow diagnosis, or a failure to keep precise records or to report cases, the number of brucellosis cases may actually be four times higher than the rate found here (Mostafavi and Asmand, 2012; Radolf, 1994; Purwar, 2007; Samaha et al., 2008). In other words, there may actually have been 200 000 cases of the disease during the study period.

This research into the trends associated with the disease showed a decrease in its incidence. Specifically, the brucellosis incidence rate was over 100/100 000 in 1989 (Benkirane, 1999), while in 2013 it was reduced to 23.8/100 000 (Pappas et al., 2006). However, the rate reported in the previous study was considerably lower than that found in most other recent research. For instance,

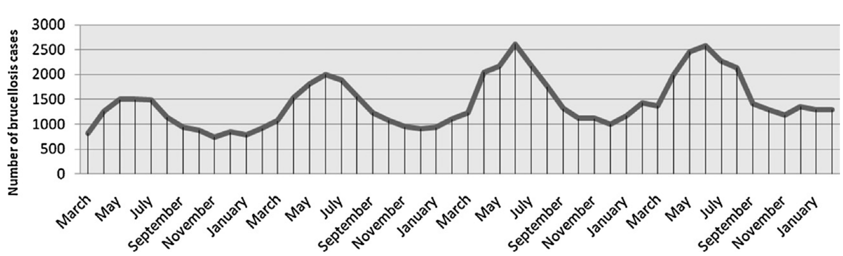

Figure 1. Time trend of brucellosis in different months of the year during 2011–2014.

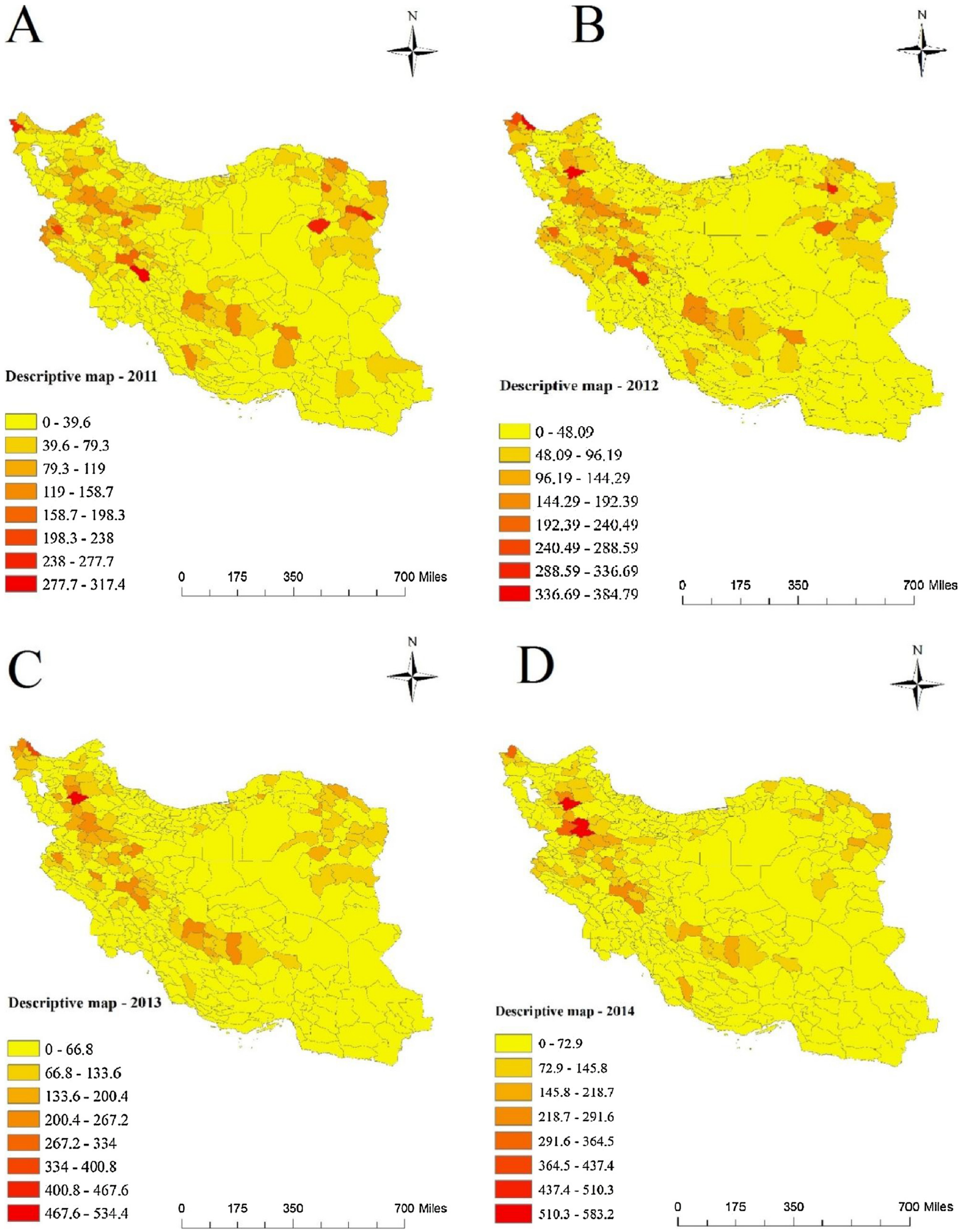

Figure 2. Distribution of brucellosis incidence rate during 2011–2014.

the present study found that the average annual incidence rate of the disease was 38.67/100 000 over the country as a whole, which is consistent with the results of other studies (Mostafavi and Asmand, 2012; Zeinali et al., 2009). Nevertheless, given that just a small percentage of brucellosis cases are diagnosed in Iran (Mostafavi and Asmand, 2012; Ramin and MacPherson, 2010;

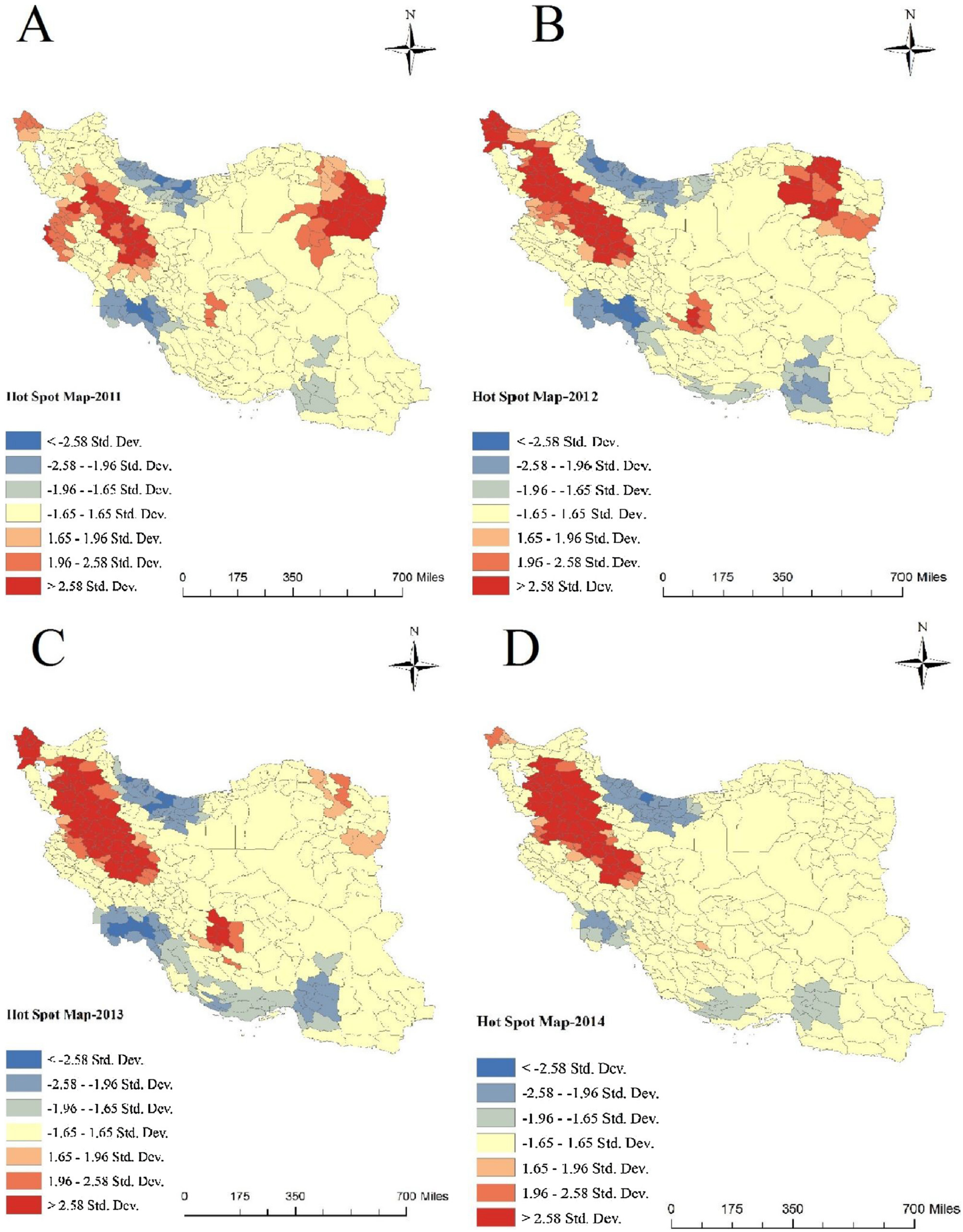

Figure 3. Hot-spot map of brucellosis incidence rate during 2011–2014.

Haran et al., 2011), the actual incidence rate of the disease is likely to be considerably higher than the number of reported cases recorded here.

On comparing the incidence rate of brucellosis in Iran with those in other countries, it was found that the incidence rate of the disease was much higher in Iran than in America and most

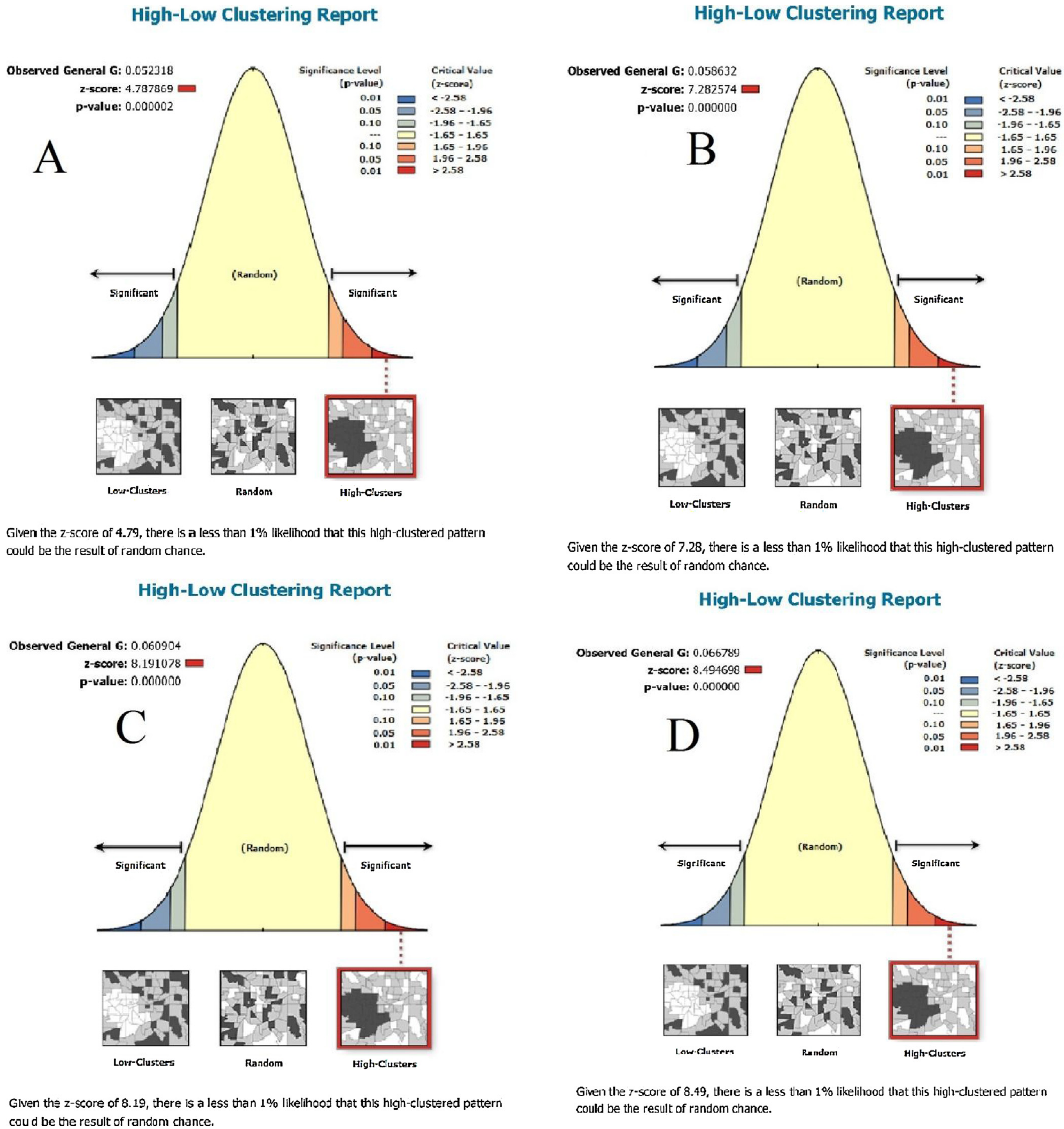

Figure 4. High-low clustering of brucellosis incidence rate during 2011–2014.

European countries (Ministry of Health, Portugal, 2017; Ministry of Health, Italy, 2017; World Organisation for Animal Health, 2017a; World Organisation for Animal Health, 2017c), but was similar to the rates in many other countries of the Middle-East, such as Saudi Arabia (World Organisation for Animal Health, 2017b), United Arab Emirates (United Arab Emirates Ministry of Health, 2017), Turkey and Iraq (World Organisation for Animal Health, 2017c). It appears that this disease is endemic in the Middle-East region. The uneven distribution of the disease may be due to a number of different reasons, including poor economic conditions and a lack of development in these countries (Pappas et al., 2006). These conditions have also made farming one of the largest industries, which along with the traditional use of non-pasteurized dairy products, increases the chances of exposure to Brucella.

The disease incidence rate also showed a clear seasonal pattern. This research found that the incidence rate increased in the early spring to mid-summer, after which there was a decrease in the number of cases, with the lowest rate being in early winter. This seasonal pattern has also been reported in a number of other studies (Awad, 1998; Eini et al., 2012; Mostafavi and Asmand, 2012;

Minas et al., 2007; Hasanjani Roushan et al., 2004). The high incidence rate of the disease in spring and summer is mainly due to the fact that it is the calving season for livestock, meaning that the chances of exposure to a placenta (or other fluids encountered during delivery that are capable of disease transmission), increases during that period (Awad, 1998). Also, the consumption of raw dairy products increases during this season, which also increases the chance of contracting brucellosis (Awad, 1998; Eini et al., 2012; Mostafavi and Asmand, 2012).

The choropleth maps of brucellosis revealed that the incidence rate of this disease was highest in cities within the vicinity of the Zagros Mountains. Koohrang County of Chaharmahal-Bakhtiari Province and Charuymaq County of East-Azerbaijan Province, which had the highest incidence rates of the disease, are both located in this area. In this study, hot-spot analysis was employed to identify the high-risk areas, which may arguably be the most important finding of this study.

According to the hot-spot analysis, the high-risk areas at the beginning of this study were concentrated more in the north-east, west, and north-west cities of Iran. However, at the end of the study, most of the high-risk areas for the disease were located in the west and north-west of the country. The high incidence rates for this disease in these areas have also been observed in several other studies (Zeinali et al., 2009; Mostafavi and Asmand, 2012). Previous research found that the provinces of Lorestan, Hamedan, Kermanshah, Kurdistan, and East-Azerbaijan had the highest incidence rates of the disease, which is consistent with the present study findings (Zeinali et al., 2009; Mostafavi and Asmand, 2012). However, all of the previous studies mentioned reported cases at the province or district level, while the present study is the first in Iran to be performed at the city level.

In support of the findings of the hot-spot analysis, it should be noted that the cities with the highest incidence rates were all in the vicinity of the Zagros Mountains. Furthermore, due to the dense oak forests and fertile soil, the main economic activity in the area is animal farming, and the Zagros Mountains are also the route of seasonal migration for nomads. Several studies have also reported a higher density of sheep and goats in these areas, which again increases the risk of brucellosis (Mostafavi and Asmand, 2012). Finally, previous research has also reported a higher rate of this disease in fertile and green lands at 800–1600 m above sea level, which is also the case in this area of Iran (Li et al., 2013). Considering the above, it should not be surprising that higher rates of brucellosis were found in the cities near the Zagros Mountains.

Another finding of this study was the clustering pattern of the disease: the areas with high incidence rates were in close proximity and had clustering distribution patterns. The clustering behavior of brucellosis has been observed in several other studies (Abdullayev et al., 2012; Zhang et al., 2014; Mollalo et al., 2014). As found in the study by Mollalo et al. (2014), this disease clustering occurred in the north-west and west of the country. This behavior of the disease may be because of environmental and/or geographical factors. Low altitudes and moderate moisture create zones with vegetative cover, and the climate conditions provide an appropriate environment for the survival and expansion of the disease. Indeed, underdevelopment or a lack of health infrastructure, as well as the traditional life style, could also be important factors in disease transmission.

Thus, the effects of geographical factors on the occurrence of zoonotic diseases are undeniable. However, the present researchers did not have access to this information, which is possibly the most significant limitation of this study. Furthermore, it was not possible to investigate the demographic characteristics of the population and so the effects of these factors were not investigated, which is another study limitation. Nevertheless, investigating the distribution of this disease and determining high-risk areas at the city level were the most important findings of the study, as this type of research had not been conducted before in Iran.

In general, it may be concluded that there are substantial differences in the spatial distribution of this disease in Iran. High incidence rates of brucellosis are found in the cities of the west and north-west of the country, and as a health issue this disease has caused many problems for the residents of these areas. The higher rate of the disease in summer has led to an increase in health costs for the residents of these areas during this season. Hence, it is necessary to accurately identify the environmental, economic, and social factors affecting the disease in order to obtain an accurate understanding of where the areas of highest risk are and when this risk is highest. This will enable the necessary authorities to ensure that there is an adequate supply of health programs and other types of support.

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Data sharing statement

No additional data are available.

Conflict of interest

None declared.

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