Original Article | J Adv Med Biomed Res. 2020; 28(130): 247-252

Journal of Advances in Medical and Biomedical Research | ISSN:2676-6264

Determining the Incidence Rate and Risk Factors of Brucellosis in Zanjan Province (Iran) from 2012 to 2017: A Spatiotemporal Analysis

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Article Info

10.30699/jambs.28.130.247

Received: 2019/09/06;
Accepted: 2020/09/16;
Published Online: 21 Sep 2020;

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ABSTRACT

Background & Objective: Zanjan is reported as a hotspot region of brucellosis infection in Iran. This longitudinal study aimed to determine the epidemiologic pattern, as well as the risk of brucellosis by using geospatial estimation in Zanjan province.

Materials & Methods: The data used in this study were collected from health centers in Zanjan province from 2012 to 2017 after obtaining the approval of the Committee of Fighting Infectious Diseases. This longitudinal study was used to determine the annual pattern of the disease and identify high-risk areas using Moran's statistics, and then was analyzed using the spatiotemporal Cox model.

Results: This research showed that the number of affected people in the province was increased after 2012, and the maximum number was observed from 2013 to 2014. However, from 2015 to 2016, there was a significant decrease. Spatial variations showed that the incidence of the disease increased in all areas over these six years. The temporal variations indicated that, from 2012 to 2017, the incidence of brucellosis in spring and summer was higher than in other seasons; thereafter, the incidence peak was witnessed in June, July, and August.

Conclusion: The results of this study can be used to determine the starting point of future programs and evaluate their effectiveness.

Keywords: Brucella infection, Geospatial, Longitudinal, Trend, Iran

Introduction

Brucellosis is the most common zoonotic disease among humans and animals; it is also known as undulant fever, wavy fever, Malta fever, and Mediterranean fever (1). Brucellosis is caused by the Brucella species of bacteria and presents itself as acute, under acute, and chronic categories. The disease is transmitted through direct or indirect contact between humans and infected animals. It has gained attention from both economic and health prospects because of miscarriages in animals (barrenness), reductions in milk production, and economic losses of infected livestock. In addition, it causes intense side effects in patients, including fever, malaise, weakness, and weight loss. The infected milk and other dairy products from animals are the most widespread source of oral transmission of Brucella (1).

About 500,000 new cases and 14×10^5 deaths are reported by the World Health Organization (WHO) each year; the Mediterranean countries are considered as high-risk regions (2). In Iran, 68,493 cases were reported from 2011 to 2014, with an incidence rate of 38.6 per 100,000 people (3). In addition, Zanjan province is estimated as a region with a high incidence rate (21–30 per 100,000 in 2010). Therefore, health care professionals, mainly those in developing countries, need modern technologies to confront numerous illnesses and deaths in order to be able to study the role of space in generating and spreading infectious diseases. Considering countries' inabilities to restrict the spread of brucellosis and manage it, scientific evaluations to improve our conception of biology and human behavior can lead us to better manage and control the disease.

The brucellosis incidence rate depends on time and region, whereas the different distributions of disease and incidence rates are reported the provinces in Iran (1, 3). Studies have estimated spatiotemporal patterns of disease distribution in Iran and throughout the world by using different methods (2–5). However, there is no study regarding the brucellosis distribution using these methods in Zanjan province. The autoregressive integrated moving average (ARIMA) model is a widely used model that can use past and present information to predict the future. The ARIMA model (5, 6), geographic information systems (GIS), spatial weights empirical Bayes smoothing (7), and scan statistics (8) have been applied to predict spatiotemporal models.

The literature has reported some limitations of these methods, including the false discovery rate due to multiple testing, length of the scan window, and selection of the number of clusters (9, 10). Accounting spatial correlations or structured heterogeneity can help assess interactions between time and area to obtain accurate estimates of risk distributions (11, 12). Currently, there are no standards to describe the disease in a spatiotemporal way. The present study offers a new approach to tackling the problems identified in the previous studies and attempts to improve the methodology of future studies.

A spatiotemporal estimation of brucellosis incidence rates has not yet been investigated by using this approach in Zanjan province, which is a high-risk region, and there are substantial knowledge gaps regarding its incidence rate. The present study aims to (1) provide a pattern of brucellosis distribution during a six-year period in urban and rural regions of Zanjan province using a mapping analysis model and (2) estimate the trend of brucellosis incidence rates from 2012 to 2018.

Materials and Methods

This longitudinal study was conducted using confirmed brucellosis cases in Zanjan province from 2012 to 2017. Zanjan lies 298 km north-west of Tehran. It has an area of 21,773 km², includes 430,871 inhabitants, and comprises 71 rural and 44 urban regions. The 2,829 brucellosis infected cases in the province were confirmed by the Health Deputy Department of Zanjan University of Medical Sciences and utilized for analysis. The data used in this study were collected from the health centers of Zanjan province over six years. They were used for the study after gaining the approval of the Committee of Fighting Infectious Diseases.

It was essential to account for the local and temporal autocorrelation patterns in the data analysis to make statistically unbiased estimates of the parameters in the geographical and trend analyses. The spatiotemporal Cox model holds the assumption of variance inflation, in which incidence rates are dependent among times and neighbors. The brucellosis incidence rate was estimated based on the population at risk in each region. The global Moran's I and Anselin Local Moran's I were used to account for autocorrelation patterns across regions. Moran's I was used to estimate the degree of dispersion in space.

In this study, the spatiotemporal model was used per the following formula (13-17).

$$\Lambda (x, t) = \lambda(x) (t) R (x, t).$$

Results

In total, 2,829 cases of brucellosis were notified from 2012 to 2017, whereas the estimated incidence rate was 44.6 per 100,000 people during the study period. Table 1 shows demographic distribution data concerning brucellosis from 2012 to 2017, separated by cities, areas, gender, and occupations. Figure 1 shows developing spatial patterns and spatial distribution of brucellosis according to the number of patients in Zanjan city using ArcGIS 10.3.

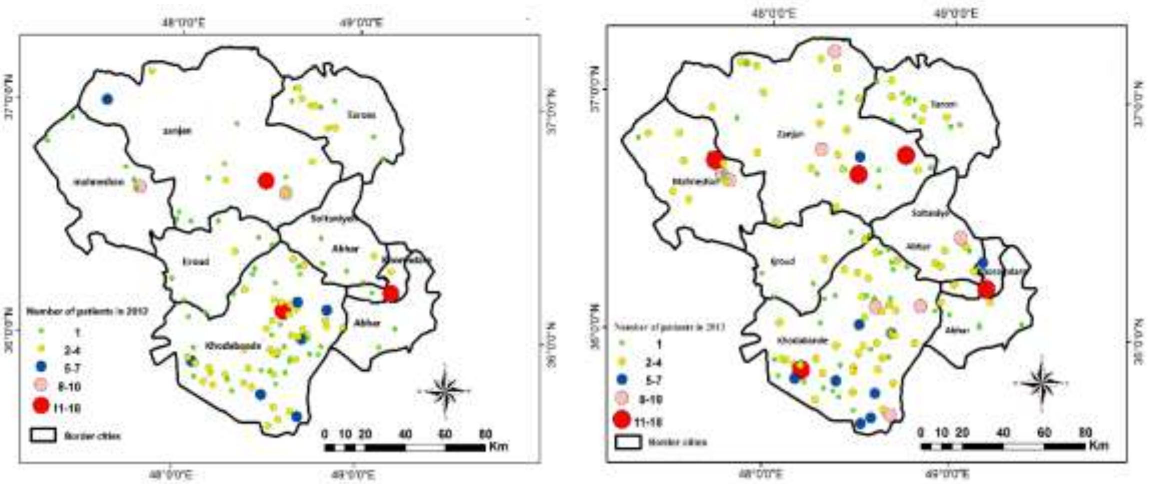
Table 1. Demographic distribution data concerning brucellosis during 2012–2017

	Region	2012	2013	2014	2015	2016	2017
Cities	Abhar	7	31	46	32	18	15
	Ijroud	12	9	27	48	24	17
	Khodabande	162	177	227	195	224	162
	Khormdare	16	24	24	28	12	18
	Zanjan	46	107	177	120	162	143
	Tarom	21	22	17	39	22	10
	Mahneshan	13	45	64	107	65	46
	Soltaniyeh	0	0	2	19	14	13
	Total	277	415	584	588	541	424
Occupations	Livestock Farmer	22.59	35.31	26.03	49.09	42.96	32.55

	Region	2012	2013	2014	2015	2016	2017
	Farmer	14.61	12.11	16.09	4.78	5.37	11.32
	Housekeeper	37.08	25.51	33. 9	23.58	33.7	34.67
	Student	7.86	11.6	12.33	9.23	6.85	3.54
	Child	2.25	3.86	3.59	3.58	1.67	2.59
	Other	8.61	11.6	8.05	9.74	9.44	15.33
Areas and gender	Urban Male	31	34	41	55	30	39
	Urban Female	18	25	51	27	36	36
	Total	49	59	92	82	66	75
	Rural Male	125	220	293	295	259	196
	Rural Female	101	122	199	211	216	154
	Total	266	342	492	506	475	349

Table 2. Generalized Additive Model (GAM) model for spatial and temporal changes of brucellosis during six years in Zanjan province

		Assessment	Confidence interval % 95	P-value
Special	Experience of consuming unpasteurized dairy products	-0.274	-45.364 44815	0.9904
	Occupation	1.378	-5.482 8.238	0.693
	County	7.825	2.658 12.993	0.003
	Area	15.322	-10.585 41.230	0.246
Temporal	Year of record	215.4	1.929 237.88	2e-16
	Experience of consuming unpasteurized dairy product	180.4	0.1793 342.91	`0.0296
	Vaccination record of livestock	-754	-8.246 -683.32	2e-16
	Record of touching livestock	-0.288	-1.474 0.896	0.632
	Occupation	-0.216	-0.4837 0.0501	0.111
	Gender	-0.0241	-0.7086 0.660	0.944



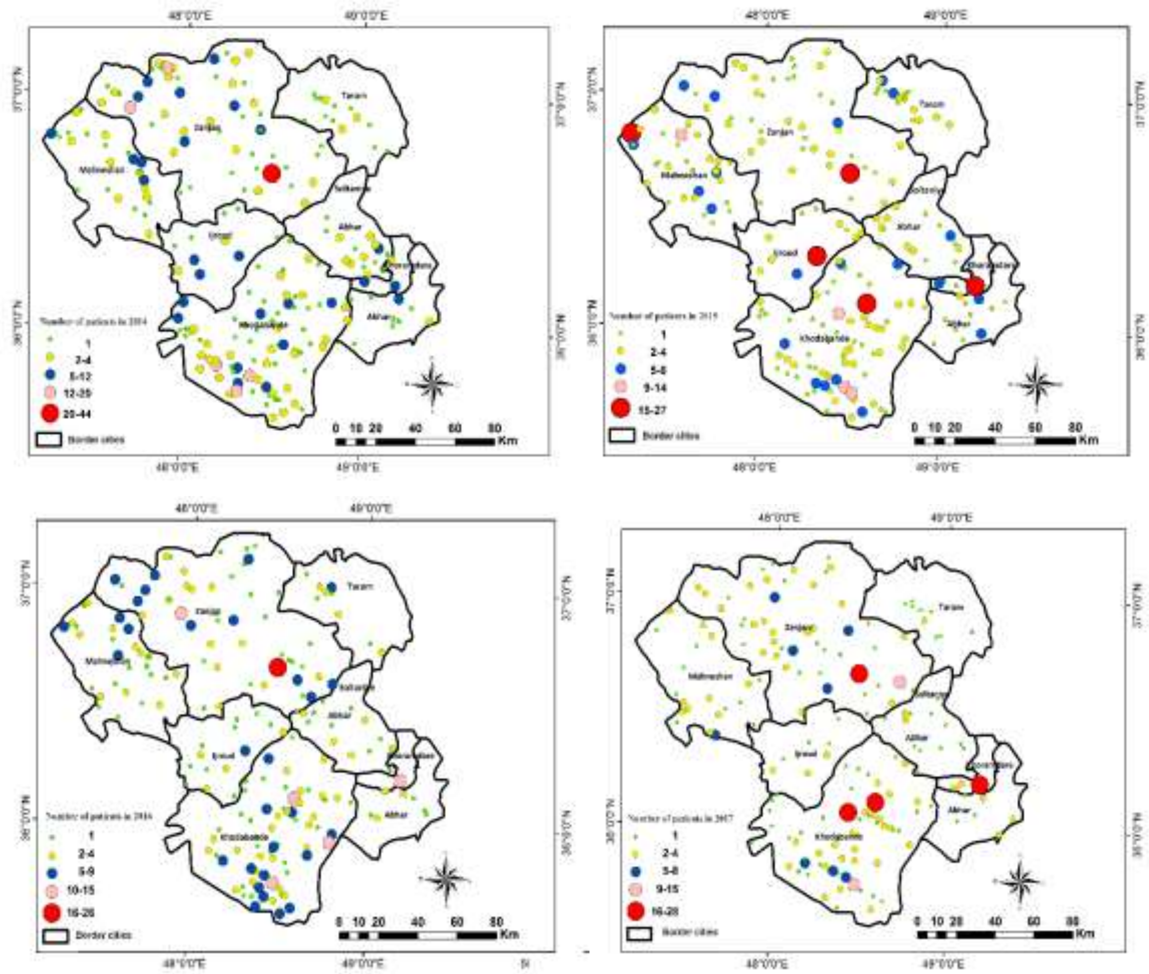


Figure 1. Spatial distribution of brucellosis incidence risk by time from 2012 to 2017

Spatial analysis (spatial variations) indicated the fact that the incidence of the disease in different cities of the province in urban and rural areas grew significantly. As can be seen in Table 1, Khodabandeh city (which had the highest number of sick people, with 162 cases in 2012) had a significant increase to 227 cases in 2014 (14%) and a decrease to 162 cases in 2017 (83%). In Zanjan city, there were 46 sick cases in 2012, which increased to 177 cases in 2014 (284%) and then decreased to 142 cases in 2017 (119%). In Mahneshan, there were 13 sick cases in 2012, which increased to 107 in 2015 (238%) and then decreased to 46 cases in 2017 (70%). Moreover, in Abhar, there were seven sick cases in 2012, which increased to 46 cases in 2015 (576%) and then decreased to 15 cases in 2017 (46%). Also, in other cities of the province, an increased number of infected patients with brucellosis was seen after 2013 (Tables 1 and 2).

A temporal (seasonal) trend analysis demonstrated the significant role of unpasteurized dairy products and livestock vaccination. It also showed that, from 2012 to 2017, the incidence of brucellosis in spring and summer was higher than in other seasons; thereafter, the incidence peak was witnessed in June, July, and August (Table 2).

Discussion

Considering the temporal and spatial aspects of brucellosis incidence, this study aimed to identify high-risk areas and determine the effectiveness of current brucellosis control programs using Moran's Local methods. We examined 2,829 cases of human brucellosis, prepared by the Infectious Diseases Department of the Ministry of Health, Treatment, and Medical Education in the study. The temporal and spatial model revealed the evolution of the disease, as it increased in some regions over the six-year study period. It also revealed an increase in brucellosis incidence in spring and summer when compared to other seasons.

According to research done by Pakzad *et al*., the incidence of brucellosis gradually increased from the early spring to the midsummer and then dropped and reached its lowest point in the early winter (3). According to Rezamirnejad *et al*., a pronounced seasonal fluctuation shows that the number of cases in spring and summer was more than those in autumn and winter (18). In Hashtarkhani *et al.'s* study, the incidence of the disease peaked from May to September (19).

In a study done by Seyedalizadeh *et al*., the disease rate increased in the warmer months of the year (i.e., during spring and summer), and it reached its peak in July **(20)**. In Ahmadkhani *et al.'s* study, the disease prevalence was on an upward trend since February and reached its peak in June before dropping at the end of the year. Similar seasonal patterns have also been observed in other studies. On the other hand, the results show that the incidence of the disease is positively correlated with temperature and evaporation and negatively correlated with precipitation **(21)**.

In a study conducted by Mohammadi *et al.*, in Zanjan province, the correlation between temperature and the number of patients with brucellosis was found to be 13%, the correlation between humidity and the number of patients was found to be 3%, the correlation between rainfall and the number of patients was found to be 5%, and the correlation between wind and the number of cases was found to be 9% **(22)**. Also, in a study by Seyedalizadeh *et al.*, there was a correlation between the incidence of the disease and temperature and altitude **(20)**. This could explain the increased number of patients in spring and summer.

Conclusion

In general, according to our results, controlling brucellosis in Zanjan province requires reviewing and designing a dynamic control program with the additional coordination of relevant institutions and organizations.

To identify high-risk periods and areas, the use of spatial and temporal analysis methods is necessary for future control programs as a starting point for the implementation of desired programs and avoiding waste of resources.

It is impossible to examine all people infected with the disease regarding private doctors (prescribing outside the clinic or hospital) and diagnostic errors. Another limitation that may have influenced the research results is the lack of an accurate and thorough registration of the data.

Acknowledgments

This paper is dedicated to the memory of Professor Soghrat Faghihzadeh. This work had the ethics code IR.ZUMS.REC.1396.311 and was supported by the grant A-11-724-7 of Zanjan University of Medical Sciences. The authors are grateful to the staff of the Health Deputy Department of Zanjan University of Medical Sciences for their work, suggestions, and data gathering that have led to significant improvement of this manuscript.

Conflict of Interest

Authors declared no conflict of interest.

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How to Cite This Article:

Rostame Z, Faghihzadeh S, Taghilou B, Khosravi Y. Determining the Incidence Rate and Risk Factors of Brucellosis in Zanjan Province (Iran) from 2012 to 2017: A Spatiotemporal Analysis. J Adv Med Biomed Res. 2020; 28 (130) :247-252