Iran J Public Health, Vol. 53, No.6, Jun 2024, pp.1446-1456

Original Article

Spatial Epidemiology and Temporal Trend of Brucellosis in Iran Using Geographic Information System (GIS) and Join Point Regression Analysis: An Ecological 10-Year Study

Sajjad Rahimi Pordanjani [1], Elaheh Mazaheri [2], Farshid Farivar [3], Masoudeh Babakhanian [4], Hasan Askarpour [5], *Somayeh Derakhshan [6]

1. *Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran*
2. *Health Information Technology Research Center, Isfahan University of Medical Sciences, Isfahan, Iran*
3. *Network Developing and Health Promotion, Health Deputy of Semnan University of Medical Sciences and Health Services, Semnan, Iran*
4. *Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran*
5. *Department of Disease Management, Deputy of Health, Yasuj University of Medical Sciences*
6. *Department of Epidemiology, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Email: Somayeh452derakhshan@gmail.com

(Received 09 Jul 2023; accepted 14 Sep 2023)

Abstract

Background: Brucellosis is one of the common diseases between humans and animals. We aimed to assess the annual incidence rate, the geographical distribution of Malta fever using GIS and its time trend.

Methods: This was an ecology study carried out in exploratory mixed design. The study population was the individuals with brucellosis in Iran during the years 2009-2018. Data analysis has been done using Joinpoint regression analysis and GIS at a significant level of $\alpha = 0.05$.

Results: The average annual incidence rate of the disease rate was 19.91 per one hundred thousand people. The trend of the changes in the incidence between 2009 and 2018 has increased and the Annual Average Percent Change increased by 4.6%. However, a joinpoint was observed in 2014 and the incidence has changed significantly at this point in time, so that the annual incidence of the disease has increased more strongly between 2009 and 2014 (APC=17.1%) and then from 2014 to 2018, the incidence of the disease has decrease (APC=-9.2%). The spatial distribution showed that the western and northwestern provinces have high incidence rate, but the northern and southern provinces have low incidence rate.

Conclusion: The incidence of brucellosis in Iran is higher than in developed countries and similar to developing countries. Ten-year trend of disease incidence increased slightly, but it has decreased in recent years. It is necessary to improve the surveillance system and increase facilities for prevention and treatment in the high-risk areas including the west and northwest of Iran.

Keywords: Brucellosis; Incidence; Average annual percent change; Geographical information system; Iran

Introduction

Malta fever or brucellosis is one of the common zoonotic disease that usually transmitted to human by infected livestock and consuming non-pasteurized dairy products(1). *Brucella melitensis* is the most common and acute pathogen that can cause various symptoms such as sudden tremors, and create general body pains (2).

Malta fever has a high prevalence in developing countries, and due to the lack of appropriate monitoring and control programs, its incidence rate has increased recently (3). This disease carries a large economic burden and causes considerable socio-health complications in endemic areas. Brucellosis causes about 500,000 cases annually all over the world (4).

Iran is the fourth country in the world where Malta fever is endemic (5). Due to the large number of nomads, traditional livestock breeding methods, as well as lack of timely vaccination of livestock, Malta fever is still one of the most important communicable diseases in Iran. In Iran, 16,000 cases of Malta fever are reported annually (6, 7).

In order to understand the epidemiology of diseases, how diseases are transmitted, identifying the pathogen, source, reservoir, incubation period, ways of prevention and treatment in order to reduce the prevalence, we must first increase our awareness about the spatial distribution and time trends of the diseases. Place and time are two important factors in the spread of brucellosis (8).

Few studies in Iran have investigated the epidemiology of brucellosis (9), so this study was conducted to determine the temporal trend and spatial distribution of brucellosis in Iran during the years 2009-2018 so that appropriate health interventions can be made to prevent new cases in the coming years and in provinces with high risk of the disease.

Methods and Materials

Study type and design

This study was an ecological study that was carried out by exploratory mixed design. Exploratory means that these types of studies explore and describe spatial patterns and temporal trends of the occurrence of the diseases. Moreover, the meaning of mixed is that in these studies, the effect of location (multiple-group study) and the effect of time (time-trend study) is simultaneously evaluated and measured (10, 11).

Sources of data collection

Three types of data were used in this study, including: 1) data related to patients obtained from Infectious diseases atlas of Ministry of Health and Medical Education. 2) Data related to the population of the provinces taken from the Statistical Center of Iran. 3) Data related to the geographic coordinate of the patients. After data collection, the data were cleaned, and finally these three sources were merged and entered in the data analysis.

Geographical setting and description of the Study Area

Iran is a country in southwest of Asia with an area of 1,648,195 km^2 located in the Middle East region. According to the latest information published by the World Bank, its population in the year 2021 was 85,028,760 (12). The geographical setting of Iran shown in Fig. 1.

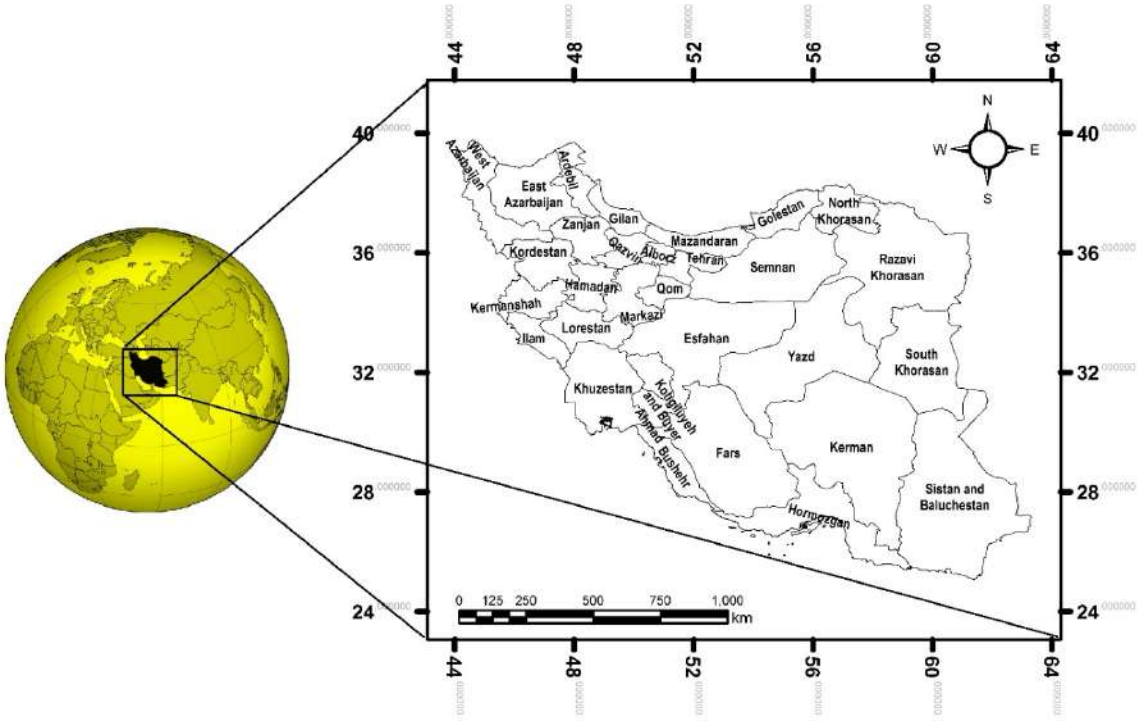

Fig. 1: Geographical setting of Iran

Descriptive analysis

The incidence rate and the average annual incidence rate of the disease per 100,000 people was used for descriptive analysis of the data. We calculated the annual incidence rate for each province in Iran for every year in the study period. Then calculated Average the annual incidence rates for all provinces each year. This the average annual incidence rate for Iran during the study period.

Temporal trend analysis

For examine the time trend of the disease, first the incidence rate and the average annual incidence rate per 100,000 people between 2009 and 2018 were obtained; then the of the time trend changes of the incidence rate was analyzed by Joinpoint regression analysis software and its latest version (Joinpoint Regression Program version 4.7.0.0 0 – Feb 26, 2019).

Joinpoint regression analysis is used to detect the trends and time points when disease incidence rates change significantly. In this study, disease incidence rate (per 100,000 people) and the frequency of brucellosis disease were considered as dependent variables and the year of diagnosis was as independent variable. Then, considering that the dependent variable followed the Poisson distribution, we used the natural log-linear model to obtain the Annual Percent Change (APC) and Average Annual Percentage Change (AAPC) values. Moreover, to determine the number and exact time of Joinpoints when the occurrence of the diseases changes significantly, Grid Search was used. The *P*-value was calculated using the Monte Carlo method with 4499 repetitions. Likewise, Bayesian Information Criterion (BIC) and Sum of Squared Errors (SEE) were used to evaluate the precision of the models and select the best one (13-15).

Spatial distribution analysis

ArcGIS software version 10.8 was used to draw the zoning of the disease incidence rates. The zoning method was based on the Natural Breaks classification system, which is a reliable Geostatistical method grouping similar values of a distribution. A Natural class is the most optimal class range found "naturally" in a data set. A class

range is composed of items with similar characteristics that form a "natural" group within a data set. In this method based on Jenks Optimization Method, the individuals or values that have the most similarities with the members of their group and the most differences with the members of other groups will set in one group.

Ethical Approval

This article is the result of a research project with ethics code IR.SEMUMS.REC.1401.200, approved by the Research and Technology Vice-Chancellor of Semnan University of Medical Sciences.

Results

Descriptive results

The total number of patients over ten years was 155,059. During the years 2009 to 2018, the average annual incidence rate of the disease was 19.91 per 100,000 people (Table 1).

Table 1: Brucellosis incidence per 100,000 people in provinces of Iran during 2009-2018

Province	*2009*	*2010*	*2011*	*2012*	*2013*	*2014*	*2015*	*2016*	*2017*	*2018*
East Azerbaijan	2.94	16.92	21.40	34.96	41.16	44.24	34.22	23.68	18.70	13.59
West Azerbaijan	31.28	24.69	34.47	56.69	56.61	51.03	44.19	33.14	37.35	44.11
Ardebil	16.93	14.87	14.90	14.62	20.29	20.06	39.97	33.69	34.37	41.96
EsfahanIsfahan	1.30	7.60	10.46	13.25	19.17	16.62	15.91	14.90	13.94	12.20
Alborz	0.00	1.11	3.19	3.40	6.41	5.25	5.21	4.83	8.75	6.86
Ilam	20.98	16.75	20.62	22.42	23.85	26.44	24.17	18.79	22.05	15.96
Bushehr	0.31	1.00	2.71	2.93	3.05	5.05	3.17	3.61	2.87	2.58
Tehran	1.57	1.33	1.52	2.00	2.51	2.71	4.07	2.87	2.43	2.09
Chahar Mahall and Bakhtiari	11.87	15.39	28.84	24.72	22.02	23.89	29.38	14.24	14.29	19.63
South Khorasan	19.58	33.60	26.50	23.27	33.20	55.04	30.88	25.62	18.44	19.32
Razavi Khorasan	20.72	28.79	32.65	35.25	42.26	40.10	35.17	29.57	39.84	47.64
North Khorasan	7.10	15.88	23.74	29.53	40.07	46.71	46.53	44.03	37.59	34.21
Khuzestan	0.00	8.62	7.35	7.38	9.54	6.81	7.34	6.01	11.32	10.12
Zanjan	25.74	22.78	27.96	30.47	43.22	59.33	56.34	51.92	40.24	38.76
Semnan	24.28	15.59	18.55	19.41	33.43	31.05	41.34	19.65	18.58	12.79
Sistan and Baluchestan	2.90	7.50	6.08	4.34	6.16	3.66	3.01	3.32	5.67	10.07
Fars	12.91	14.61	20.54	28.02	24.82	24.54	26.01	20.08	17.31	16.21
Qazvin	16.98	16.64	26.05	26.48	29.43	36.01	39.24	32.27	27.08	27.13
Qom	3.61	6.55	6.86	6.28	11.77	7.46	12.51	6.19	3.71	5.44
Kordestan	28.21	23.88	35.89	50.33	63.58	101.73	83.48	60.64	77.07	50.06
Kerman	18.43	15.66	14.32	15.96	19.15	16.56	19.20	15.86	18.04	19.26
Kermanshah	43.84	37.33	39.74	39.26	54.31	63.67	70.78	43.07	37.32	35.31
Kohgiluyeh and Buyer Ahmad	17.88	9.03	9.26	10.16	12.94	27.64	18.52	20.48	15.35	16.99
Golestan	15.37	16.34	11.14	19.16	32.52	28.66	27.41	23.92	19.28	19.31
Gilan	1.63	2.80	2.66	3.05	2.64	2.39	3.65	3.75	3.07	4.58
Lorestan	47.78	36.52	48.17	66.00	72.68	100.06	115.69	80.65	66.33	68.33
Mazandaran	10.49	14.49	14.15	18.14	16.53	11.13	12.71	12.85	13.59	13.92
Markazi	33.21	31.69	42.36	51.87	41.97	35.84	38.01	30.64	30.33	39.13
Hormozgan	2.12	2.40	1.08	1.36	1.69	1.06	0.86	1.63	1.38	1.19
Hamadan	25.11	33.54	47.49	65.22	85.60	96.28	74.91	50.80	51.14	68.98
Yazd	14.61	13.16	16.12	13.11	26.61	15.33	19.37	13.53	14.65	20.24
Average Annual Incidence Rate for IRAN	15.47	16.35	19.89	23.83	29.01	32.46	31.71	24.07	23.29	23.81

Time trend results

The results related to the trend of the disease based on the year analyzed by Joinpoint regression has been shown in Fig. 2 and Table 2.

In Fig. 2, the incidence of the disease by year has been shown. The trend of changes in the incidence of the disease during the years 2009 to 2018 has increased and AAPC has increased by 4.6%. However, a joinpoint was observed in 2014, and the incidence of the disease has changed significantly at this point in time, so that the annual incidence of the disease has increased more strongly between 2009 and 2014 (APC=17.1%), then from 2014 to 2018, the incidence has decreased (APC= -9.2%). More information about this time trend is shown in Table 2.

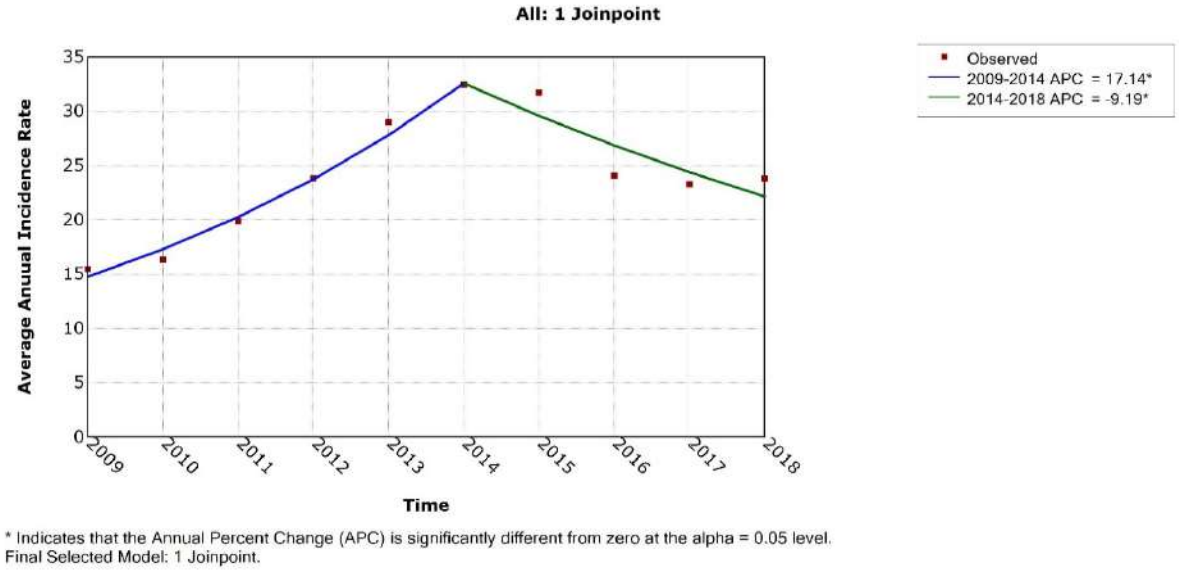

Fig. 2: Temporal analysis with joinpoint regression models fitted to Average Annual Incidence Rate of Brucellosis in Iran during 2009-2018

Table 2: More details of temporal analysis with regression models of connection point corresponding to the average annual incidence of brucellosis

Time frame	*APC*		*P-value*	*AAPC*		*P-value*
	Point estimate	95% CI		Point estimate	95% CI	
2009-2014	17.1	9.9, 24.9	<0/001	4.6	0.4, 9.0	<0/001
2014-2018	-9.2	-17.1, -0.6	<0/001			

Spatial distribution results

To analyze the spatial pattern of brucellosis, first the Incidence Rate of the disease was calculated during the years 2009 to 2018, and then the zoning of the disease was drawn in the GIS environment (Figs. 3 to 5).

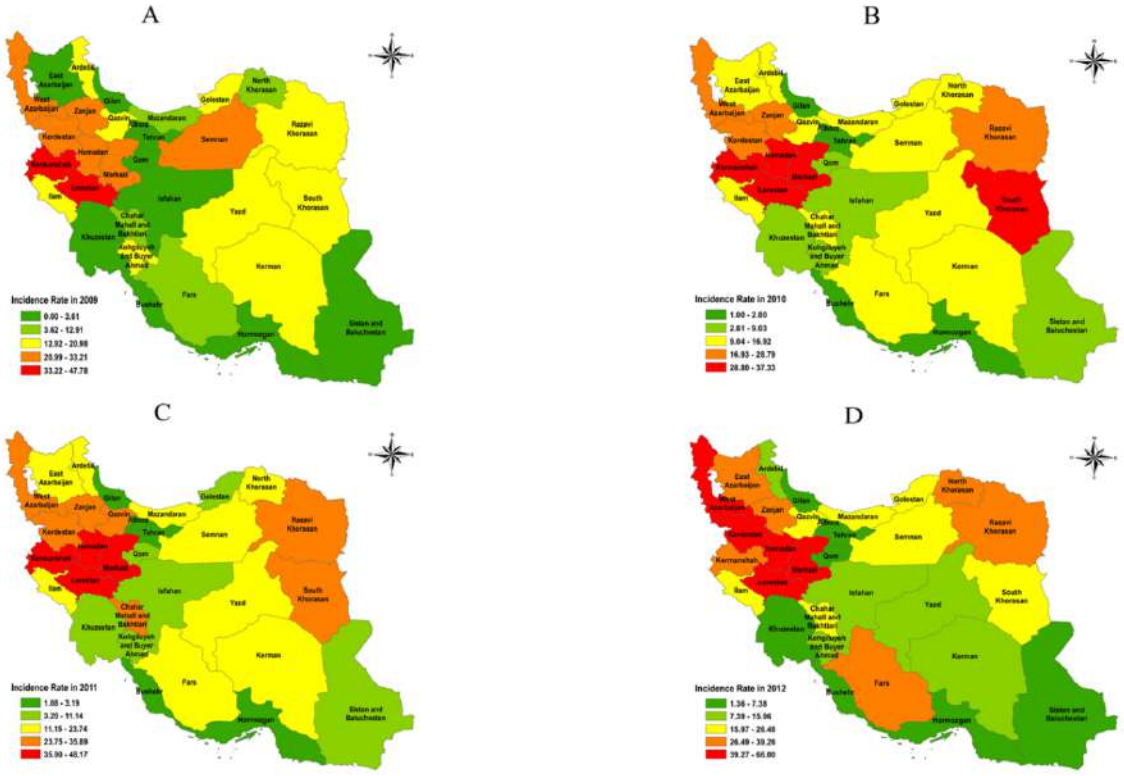

Fig. 3: Incidence of brucellosis during the years 2009(A), 2010(B), 2011(C) and 2012(D)

Figure A-3, which shows the incidence rate in 2009, the two provinces with the highest incidence rate include Lorestan (IR=47.77) and Kermanshah (IR=43.88) provinces, and the three provinces with the lowest incidence rate include Alborz Province (IR = 0), Khuzestan (IR=0) and Bushehr (IR=0.30).

Figure B-3, which shows the incidence rate in 2010, the three provinces that had the highest rate of incidence include the provinces of Kermanshah (IR=37.32), Lorestan (IR=36.52) and South Khorasan (IR=33.60) and three provinces with a lower incidence rate including the provinces of Bushehr (IR=0.99), Alborz (IR=1.11) and Tehran (IR=1.33).

Figure C-3, which shows the incidence rate in 2011, the three provinces that had the highest incidence rate include the provinces of Lorestan (IR=48.16), Hamedan (IR=47.48) and Markazi (IR = 42.36) and three provinces with lower incidence rates including Hormozgan (IR=1.07), Tehran (IR=1.51) and Gilan (IR=2.66).

Figure D-3, which shows the incidence rate in 2012, the three provinces that had the highest incidence rate include the provinces of Lorestan (IR=66.00), Hamadan (IR=65.22) and West Azerbaijan (IR=56.68) and three provinces with a lower incidence rate including the provinces of Hormozgan (IR=1.36), Tehran (IR=2.00) and Bushehr (IR=2.93).

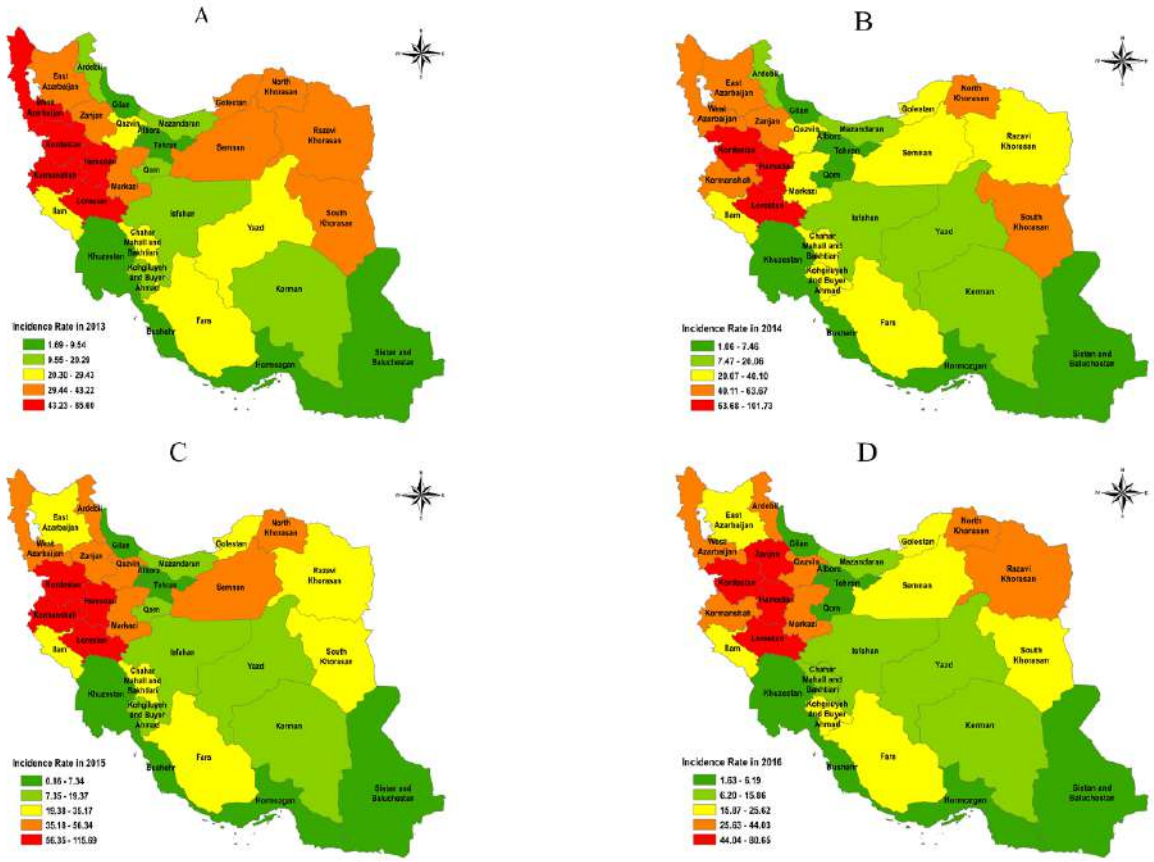

Fig. 4: Incidence of brucellosis during the years 2013(A), 2014(B), 2015(C) and 2016(D)

Figure A-4, shows the incidence rate in 2013, the three provinces that had the highest rate of incidence include the provinces of Hamedan (IR=85.59), Lorestan (IR=72.68) and Kurdistan (IR=63.58) and three provinces with a lower incidence rate including the provinces of Hormozgan (IR=1.69), Tehran (IR=2.51) and Gilan (IR=2.63).

Figure B-4, shows the incidence rate in 2014, the three provinces that had the highest rate of incidence include the provinces of Kurdistan (IR=101.73), Lorestan (IR=100.05) and Hamadan (IR=96.27) and three provinces with a lower incidence rate including the provinces of Hormozgan (IR=1.06), Gilan (IR=2.39) and Tehran (IR=2.71).

Figure C-4, which shows the incidence rate in 2015, the three provinces that had the highest rate of incidence include the provinces of Lorestan (IR=115.69), Kurdistan (IR=83.48) and Hamadan (IR=74.91) and three provinces with a lower incidence rate including the provinces of Hormozgan (IR=0.86), Sistan and Baluchistan (IR=3.00) and Bushehr (IR=3.16).

Figure D-4, which shows the incidence rate in 2016, the three provinces that had the highest rate of incidence include the provinces of Lorestan (IR=80.65), Kurdistan (IR=60.63) and Zanjan (IR=51.91) and three provinces with a lower incidence rate including the provinces of Hormozgan (IR=1.63), Tehran (IR=2.87) and Sistan and Baluchistan (IR=3.31).

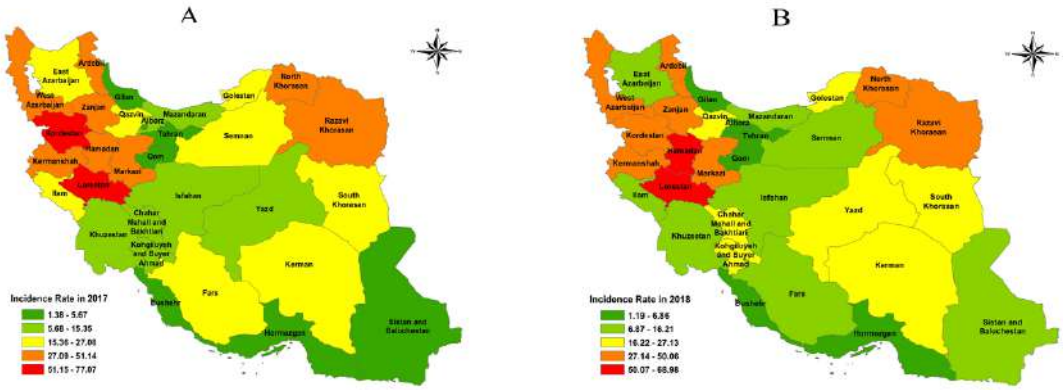

Fig. 5: Incidence of brucellosis during the years 2017(A) and 2018(B)

Figure A-5, shows the incidence rate in 2017, the two provinces that had the highest rate of incidence include the provinces of Kurdistan (IR=77.06) and Lorestan (IR=66.32) and three provinces with a lower incidence rate including the provinces of Hormozgan (IR=1.37), Tehran (IR=2.42) and Bushehr (IR=2.87).

Figure B-5, shows the incidence rate in 2018, the two provinces that had the highest rate of incidence include the provinces of Hamedan (IR=68.98) and Lorestan (IR=68.33) and three provinces with lower incidence rates including the provinces of Hormozgan (IR=1.19), Tehran (IR=2.08) and Bushehr (IR=2.58).

Discussion

The average annual incidence rate of brucellosis during the years 2009 to 2018 was 19.91 per 100,000 people. The annual average incidence of the disease in the whole country was 38.67 per 100,000 and considering that only a small percentage of brucellosis cases are diagnosed in Iran, the actual incidence of the disease is probably significantly higher than the number of reported cases (16).

A comparison of the incidence rate of Malta fever in Iran with other countries showed that the incidence in Iran is significantly higher than in developed countries such as the United States and Most European countries (17). The disease is still endemic in the countries of the Middle East, and the incidence rate has been reported high in Iran (23.8), Turkey (26.2), Syria (160.3), Saudi Arabia (21.4), as well as Iraq (27.8). However, in many countries, the incidence is very low per 100,000 people such as United States (0.04), Italy (0.9), Spain (1.3), Russia (0.4), Chile (0.006) and France (0.05) (18). Uneven distribution in different countries can be attributed to the low socioeconomic status and undeveloped condition in farming and ranching industry (19).

In the assessment of the time trend, we found that the disease incidence has increased by an average of 4.6% between 2009 and 2018. The incidence of new cases of the disease is increasing in Iran. The incidence of brucellosis in Iran increased from 2011 to 2014 and in 2015 compared to 2014 has decreased and its reduction in 2015 can be attributed to the increase in animal health and vaccination (17). During the 9-year study period in Iran, the incidence of brucellosis has increased between 2010 and 2014. From 2014 to 2017, there was a decreasing trend, but in the last year of the study, this trend increased again (20).

The spatial distribution of the disease in Iran during ten years showed that the western and northwestern provinces of Iran have a high incidence, the northern and southern provinces of Iran have a low incidence, and the central provinces have an average incidence. The distribution of the disease is uneven throughout the country, though some cases have been reported in all provinces of

the country; however, its prevalence is more in the western, northern and northwestern provinces, in the Zagros Mountain region (21, 22). The highest incidence of Malta fever in the years 2006-2015 was in the provinces of Lorestan, Hamadan and Kurdistan, Markazi, Kermanshah, East and West Azarbaijan and North Khorasan, South Khorasan and Razavi Khorasan (17). The results of this study were completely compatible with the results of the present study.

Differences between countries in the incidence of this disease, there are also fundamental differences within countries. For example, the incidence rate in Iraq and Egypt varies 4 to 5 times depending on the region. This highlights the influence that climate, environmental, socioeconomic, and lifestyle factors have on the disease incidence (23, 24).

In the western provinces of Iran, due to the proximity to the Zagros Mountain and the presence of clump oak forests and fertile soil, the main economic activities of the people are farming and ranching. Moreover, due to the movement of nomads, these areas have a higher rate of Malta than other parts of Iran (25). The provinces outside the Zagros Mountains, such as Qom and Tehran, the incidence rate was 7 and 10 cases per 100,000 cases, respectively (7). The studies are in line with our study and show that the incidence rate of brucellosis in the Zagros Mountains is significantly higher than other provinces, related to the high incidence of brucellosis in Iraq and Turkey (21).

The studies have stated several reasons for the high incidence of brucellosis in the Zagros region, among them, we can mention to the density of livestock in these areas. Zagros region accommodates 43% (more than 34 million people) of the total population of Iran and 52 % of the country's livestock including cows, sheep and goats. On the other hand, most of the nomadic and rural population of the country live in the Zagros Mountains and have a close contact with animals. These residents often assist in the birth of animals and are in contact with the placenta and related secretions, which are the potential agents for the transmission of *Brucella* bacteria. Other reasons include the low level of hygiene and the lack of access to antibacterial detergents and disinfectants in these areas. Besides, most population of in these rural areas, especially nomads, have insufficient training in terms of transmission, manifestations and complications of brucellosis. Among other reasons, it can be mentioned to the continuous consumption of unpasteurized, raw, and semi-raw dairy products (such as milk and cream). Due to living in impassable areas, transportation, monitoring and vaccination of grazing herds are very difficult and not very effective. Often, several breeders meet in one place and cause transmission of *Brucella* from one herd to another (26-29).

One limitation of this study was the absence of investigation and evaluation of the temporal trend and spatial distribution of brucellosis post-2018, which was attributed to the researchers' inability to access cleaned data.

Conclusion

The incidence of brucellosis in Iran is higher than developed countries and similar to developing countries and the incidence of new cases is increasing at a relatively high rate. Generally, during the years 2009 to 2018, the average annual incidence rate of the disease was 19.91 per 100,000 population. The areas with high incidence or high-risk cluster during these ten years were mostly related to the western and northwestern regions of the country, and the areas with low incidence or low-risk cluster were related to the southern and northern regions of Iran. Especially the increase of new cases and the high number of these cases in the western and northwestern regions of the country, it is hoped that the results will help to make appropriate decisions and accurately target health interventions in these regions.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or

submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgmnets

We appreciate the Ministry of Health and Medicine of Iran for their complete cooperation in carrying out the study, and acknowledge the research assistant from Semnan University of Medical Sciences for the financial support provided for this research.

Conflict of interest

There is no conflict of interest between the authors of this article.

References

1. Kamal S, Hashemi S, Nasaji M, et al (2009). Frequency of reported cases of brucellosis to province health center from public and private sectors in Semnan 2006-2007. *Koomesh,* 10 (2).
2. Mohammadian-Khoshnoud M, Sadeghifar M, Cheraghi Z, et al (2021). Predicting the incidence of brucellosis in Western Iran using Markov switching model. *BMC Res Notes,* 14 (1):79.
3. Lai S, Zhou H, Xiong W, et al (2017). Changing epidemiology of human brucellosis, China, 1955–2014. *Emerg Infect Dis,* 23 (2):184-194.
4. Mollalo A, Alimohammadi A, Khoshabi M (2014). Spatial and spatio-temporal analysis of human brucellosis in Iran. *Trans R Soc Trop Med Hyg,* 108 (11):721-728.
5. Mostafavi E, Asmand M (2012). Trend of brucellosis in Iran from 1991 to 2008. *Iranian Journal of Epidemiology,* 8 (1):93-100.
6. Pakzad I, Hosseinzadehgan H, Abtahi H, et al (2013). Human brucellosis in Iran: Incidence, complication, diagnosis, treatment and prevention. *Journal of Pure and Applied Microbiology,* 7 (2):1177-1188.
7. Mirnejad R, Jazi FM, Mostafaei S, Sedighi M (2017). Epidemiology of brucellosis in Iran: A comprehensive systematic review and meta-analysis study. *Microb Pathog,* 109:239-247.
8. Olfatifar M, Hosseini SM, Shokri P, et al (2020). How to improve the human brucellosis surveillance system in Kurdistan Province, Iran: reduce the delay in the diagnosis time. *Epidemiol Health,* 42: e2020058.
9. Mirnejad R, Jazi FM, Mostafaei S, et al (2017). Epidemiology of brucellosis in Iran: A comprehensive systematic review and meta-analysis study. *Microb Pathog,* 109:239-247.
10. Rothman KJ, Greenland S, Lash TL (2008). *Modern epidemiology*. ed. Wolters Kluwer Health/Lippincott Williams & Wilkins Philadelphia.
11. Morgenstern H (1995). Ecologic studies in epidemiology: concepts, principles, and methods. *Annu Rev Public Health,* 16:61-81.
12. Worldbank. databank (2022). Explore. Create. Share: Development Data. https://databank.worldbank.org/
13. Dragomirescu I, Llorca J, Gómez-Acebo I, et al (2019). A join point regression analysis of trends in mortality due to osteoporosis in Spain. *Sci Rep,* 9 (1):4264.
14. Pordanjani SR, Kavousi A, Mirbagheri B, et al (2021). Geographical pathology of acute lymphoblastic leukemia in Iran with evaluation of incidence trends of this disease using Joinpoint regression analysis. *Arch Iran Med,* 24 (3):224-232.
15. Alipour A, Zarghami M, Pordanjani SR, et al (2022). Spatial distribution and temporal trend of drug-related deaths in the Islamic Republic of Iran during 2014–2017. *East Mediterr Health J,* 28 (10):758-767.
16. Pakzad R, Pakzad I, Safiri S, et al (2018). Spatiotemporal analysis of brucellosis incidence in Iran from 2011 to 2014 using GIS. *Int J Infect Dis,* 67:129-136.
17. Shirzadi MR, Mohammadi P, Moradi G, et al (2021). The incidence and geographical distribution of brucellosis in Iran using geographic information system and prediction of its incidence in 2021. *J Prev Med Hyg,* 62 (3):E635-E634.
18. Pappas G, Papadimitriou P, Akritidis N, et al (2006). The new global map of human brucellosis. *Lancet Infect Dis,* 6 (2):91-99.
19. Dean AS, Crump L, Greter H, et al (2012). Global burden of human brucellosis: a systematic review of disease frequency. *PLoS Negl Trop Dis,* 6 (10):e1865.

20. Khalilian M-S, Ramazanpour J, Hosseini SM, et al (2021). Trends of human brucellosis in Central Iran (2010–2018). *J Res Med Sci,* 26:55.
21. Abdi M, Mirzaei R, Lohrasbi V, Zamani K (2020). Zagros Mountains: a region in Iran with extremely high incidence of Brucellosis. *Infect Control Hosp Epidemiol,* 41 (3):380-382.
22. Karimi S, Fallah S, Olfatifar M, et al (2020). Spatiotemporal analysis of brucellosis cases in Golestan province from 2015 to 2017 years using Geographic Information System. *Journal of Zoonotic Diseases,* 4 (1):17-27.
23. Hotez PJ, Savioli L, Fenwick A (2012). Neglected tropical diseases of the Middle East and North Africa: review of their prevalence, distribution, and opportunities for control. *PLoS Negl Trop Dis,* 6 (2):e1475.
24. Khazaei Z, Goodarzi E, Naemi H, et al (2020). COVID-19 pandemic in the world and its relation to human development index: a global study. *Arch Clin Infect Dis*, 15(5):e103093.
25. Khazaei S, Shojaeian M, Zamani R, et al (2016). Epidemiology and risk factors of childhood brucellosis in West of Iran. *Int J Pediatr,* 4 (7):2099-2104.
26. Corbel MJ (2006). *Brucellosis in humans and animals*. ed. World Health Organization.
27. Esmaeili H (2014). Brucellosis in Islamic republic of Iran. *J Med Bacteriol,* 3 (3-4):47-57.
28. Honarvar B, Moghadami M, Lankarani K, et al (2017). Brucellosis as a neglected disease in a neglected population: a seroepidemiological study of migratory nomads in the Fars province of Iran. *Epidemiol Infect,* 145 (3):491-497.
29. Franc K, Krecek R, Häsler B, et al (2018). Brucellosis remains a neglected disease in the developing world: a call for interdisciplinary action. *BMC Public Health,* 18 (1):125.