Spatial Distribution and Epidemiological Factors of Brucellosis in Northwest of Iran.

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Research Article

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Abstract

**Background:** Brucellosis is one of the most prevalent infectious diseases in the world that infected humans directly through contaminated livestock or indirectly through animal products and induces high medical and economic damage annually. We extracted the incidence cases of the disease from 2016 to 2020 in this retrospective cross-sectional study using the disease registration system of Ardabil University of Medical Sciences. The interpolation method and IDW model were employed for spatial analysis and disease distribution and determination of hotspot points, Moran I and General G analysis were used to determine the type of distribution and spatial autocorrelation at a significant level (P <0.05). GIS software 10.4.8 was applied to determine areas.

**Results:** 2679 cases of brucellosis were diagnosed in the province during the study that 96.97% were Iranian, 2.95% Azerbaijani, and 0.08% were Iraqi. 40.5% of patients were female and 59.5% male. The highest numbers of infected cases were reported in 2020 with 29.2% and the lowest number was reported in 2016 with 16%. Rural areas had a high prevalence in terms of distribution and the north of Aslanduz and the central part of Sarein were determined as two significant rural fauci of the disease. The trend of disease was increasing from east to west of the province.

**Conclusion:** Brucellosis is very widespread in rural areas in Ardabil Province. Ardabil University of Medical Sciences is required to take practical and educational measures to control this disease in high-risk centers. It is expected to take measures in order to educate villagers.

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**Background**

Brucellosis is one of the most prevalent Zoonosis infectious diseases in the world that infected humans directly through contaminated livestock or indirectly through animal products and induces high medical and economic damage annually [1]. The brucellosis is caused by a pathogenesis agent that is a small, gram-negative aerobic, immobile, capsule-free, capsule-free, bacillus called Brucella that six species have been identified so far [2] and two species are very prevalent in Iran: *Brucella melitensis* and *B. abortus* [3]. The incubation period of this disease is 1 to 2 months, which is appeared by extended fever, body aches, night sweats, general weakness, and arthralgia [4]. Consuming raw milk or unpasteurized cheese infected with a bacterial agent and to some extent, contact with infected animals transmit human infections [5]. Farmers, shepherds, slaughterhouses, butchers, and veterinarians have been considered high-risk professions [6]. The disease is detected in many parts of the world, but the Mediterranean region, Arabian Peninsula, Indian subcontinent, and parts of the central and southern United States reported the highest cases [7–8]. Iran reports the mean prevalence rate of the disease as 21 per 100,000 people, but the prevalence of the disease has been reported from 1.5 to 107.5 per 100,000 people in different geographical regions [9–10]. Brucellosis is one of the most prevalent zoonotic diseases that caused to die more than 611 people and its yearly mortality rate is near to 971 thousand people [11]. This disease is still endemic in Iran. Iran has the fourth rank in the world and first rank in the Eastern Mediterranean region in terms of Brucellosis outbreak [12–13]. There are some new methods to identify the high-risk
locations to outbreak the disease such as using Geographic Information System (GIS) software that can help to manage the disease, develop preventive plans and control the diseases by providing the map of disease distribution, determining the spatial-temporal correlation, and determining the disease hotspots [14–15]. We used GIS software to determine the prevalence of Brucellosis in one of the endemic provinces of Brucellosis in northwestern Iran. In this study and applied this software to determine the hot spots of the disease and the spatial correlation and type of disease distribution.

Methods

Studied area

Ardabil province is located in the northwest of Iran which has geographical coordinates of 47.8911° E and 38.4853° N. This province is a mountainous region with cold and snowy winters and moderate summers and most people operate in the livestock and agriculture fields (Fig. 1).

Data Analysis

This study was a retrospective cross-sectional research and we extracted the cases of the disease-related to 2016 to 2020 from the Brucellosis disease registration system of Ardabil University of Medical Sciences and studied them in terms of annual prevalence. The interpolation method and IDW model specialized for mountainous regions were employed for spatial analysis and disease distribution and determination of hotspot points, and Moran I and General G analysis were used to determine the type of distribution and spatial autocorrelation at a significant level (P < 0.05). To determine the regions with higher and lower clusters of the disease and the following formula was used to calculate them that all these processes were performed applying GIS 10.4 software.

\[ I = \frac{N}{W} \sum_{i} \sum_{j} \omega_{ij} (x_i - x)(x_j - x) + \sum_{i} (x_i - x) \]
\[ G = \frac{\sum_{i} \sum_{j} W_{ij} x_i x_j}{\sum_{i} \sum_{j} 1} - \frac{\sum_{i} x_i}{\sum_{j} 1} \times \frac{\sum_{j} x_j}{\sum_{i} 1} \]

Results

Epidemiological factors

2679 cases of brucellosis were diagnosed in the province during the study that 96.97% were Iranian, 2.95% Azerbaijani, and 0.08% were Iraqi. 40.5% of patients were female and 59.5% were male. The highest number of infected cases was reported in 2020 with 29.2% and the lowest number was reported in 2016 with 16% that indicates that the incidence of brucellosis has increased significantly in recent years. This disease increases from May at the same time as the birth of livestock and approaches its maximum rate in August (Fig. 2).
Spatial analysis

All ten country of the province were infected with brucellosis and Ardabil country with 37.3% had the most cases during the study and Khalkhal and Kowsar with 0.4 and 0.5% respectively had the lowest rate. 69.2% of patients lived in rural regions, 24.5% in urban, and 6.3% in nomadic regions. The results of IDW interpolation analysis explain that there are two hotspot regions in Ardabil in terms of the prevalence of Brucellosis. Aslanduz country is a high-risk region in the north of the province and its risk of infection is between 13–15%, and there is a small hot spot in the center of the province in Sarein with the risk of infection of 11-13.5%. Studying the disease trend in the province reveals that the regions that ended to the East Azerbaijan province have a high disease trend, which includes the central parts of Aslanduz, Ingot district of Garmi, Moradlu and central districts of Meshkinshahr that are regions with high-risk of disease prevalence (Fig. 3). The results of spatial correlation by Moran I (0.0900) and General G high/low clustering method (0.0821) additionally indicate that the disease distribution has a significant clustering and high clustering pattern, respectively (Fig. 4 and Table 1).

| General G Summary     | Global Moran's I Summary |
|-----------------------|--------------------------|
| Observed General G:   | Moran's Index:           |
| 0.000028              | 0.084016                 |
| Expected General G:   | Expected Index:          |
| 0.000020              | -0.027027                |
| Variance:             | Variance:                |
| 0.000000              | 0.004291                 |
| z-score:              | z-score:                 |
| 1.738086              | 1.695222                 |
| p-value:              | p-value:                 |
| 0.082196              | 0.090033                 |

Discussion

Brucellosis is one of the most common zoonotic diseases in Iran. Medical services were increased and improved in recent years, but 2679 patients have been reported during the study period in Ardabil province located in the northwest of Iran that is increasing. Men with 59.5% reported the highest incidence of Brucellosis in this study, which was similar to the results achieved by various studies, including studies conducted by Hamzavi et al. in 2014 [16] and Deno et al. in 2010 [17] that have reported that men have the highest incidence rate. Most of the men in Ardabil work in animal husbandry or in butchers and slaughterhouses, hence, they are threatened with more risks in terms of facing livestock, accordingly, men are more prone to be infected with zoonotic diseases such as Brucellosis. We observed most cases in May and June. In general, spring and summer have the highest cases of the disease and the lowest cases were observed in fall and winter. Spring and summer have the most breeding and lactation in livestock and of course, producing livestock and dairy products and the amount of contact with livestock is higher
in these seasons, consequently, these seasons have the most cases of the disease. This is in agreement with the findings achieved by many other researchers. [18–19].

Rural regions had more than 69% of patients with Brucellosis in Ardabil province. Accordingly, we can state that Brucellosis in this province causes a problem in rural areas. Villagers' lifestyle who operate in animal husbandry and agriculture and also direct contact with livestock, consuming dairy products that are traditionally prepared by themselves show that it is normal to observe the most cases of the disease in rural regions. There were more than 85% of infected cases in rural regions in Arak, which is much higher than the results achieved by this study [20], and Isfahan's rural regions also showed the highest number of cases, so that the incidence of the disease in the rural population had been about ten times of the urban population [18]. The results of additional studies in the world prove that a direct relationship is observed between the country's livestock population and their infection with human disease in many countries [21–22].

Spatial analysis of Brucellosis revealed that the disease had a spatial nature and has been distributed in clusters in the northwest of the studied region. Previous research also reveals the cluster distribution of Brucellosis in Iran and other parts of the world [23]. The results achieved by interpolation analysis of brucellosis in this study explained that there are two important centers of the disease in the province, both located in rural regions in the north and center of the province. The north of Aslanduz is the most dangerous center in terms of Brucellosis infection transmission with the risk rate of infection transmission between 13.5 to 15%. This center is a region with high and more traditional animal husbandry and 50% of the inhabitants are nomads with many livestock. Other studies, including studies conducted in China [24] and the Republic of Azerbaijan [25], have revealed that high-risk centers in terms of diseases have a direct relationship with the number of cattle kept in the region and depend completely on the job. The east to west of the province has an increasing trend of incidence of Brucellosis, which needs health and educational interventions in these areas.

Conclusion

Brucellosis is very widespread in rural areas in Ardabil and two significant rural hot spots of the disease were identified in the north of Aslanduz and in the central district of Sarein., Ardabil University of Medical Sciences is required to take practical and educational measures to control this disease in these two regions. As the results of this study explain, there is a higher incidence trend of the disease in the areas with the common border with East Azerbaijan province. Must to make required coordination with Tabriz University of Medical Sciences in this regard, and since this disease is a zoonotic disease, the animals should be vaccinated against this disease to perform veterinary measures areas.

Abbreviations

GIS: Geographic Information System; IDW: Inverse distance weight.
Declarations

-Ethics approval and consent to participate

The study was approved by the Ethics Committee of Ardabil University of Medical Sciences (IR.ARUMS.REC.1398.351). Permission to conduct the study was obtained from this committee and all patients had signed an informed consent form and all methods were performed in accordance with the relevant guidelines and regulations by including a statement in the Ethics approval.

-Consent for publication

Not applicable.

-Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due Ethics Committee of Ardabil University of Medical Sciences restrictions but are available from the corresponding author on reasonable request.

-Competing interests

The authors declare no conflict of interest.

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-Authors’ contributions

JM, SHH and EMA: Study design, Data analysis, Writing - original draft, Writing - review & editing. AAG, BN, EMA: Writing - review & editing. DE, JA and AAG: Data collection.

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References

1. Shahriari S, Ghatee MA, Haghdoost AK, Taabody Z, Khajeh Kazemi R, Parisae Z, et al. Demographic and epidemiological study of brucellosis in the Kohgilooye and Boyerahmad province, 2009-2013.
2. Aghaali M, Mohebi S, Heydari H. Prevalence of asymptomatic brucellosis in children 7 to 12 years old. Interdisciplinary Perspect Infect Dis 2015; 2015:4.
3. Armaghane Danesh 2015; 20:149-60 .2.Shabhazi Y, Afshari S, Shavisi N. The epidemiological survey of animal brucellosis in Kermanshah province. Iran J Veterinary Clin Sci 2016; 10:72-97.
4. Punda-Polić V, Cvetnić Z. Human brucellosis in Croatia. The Lancet. Infectious diseases. 2006 Sep 1;6(9):540-1.
5. Arimi SM, Koroti E, Kang’ethe EK, Omore AO, McDermott JJ. Risk of infection with Brucella abortus and Escherichia coli O157: H7 associated with marketing of unpasteurized milk in Kenya. Acta tropica. 2005 Oct 1;96(1):1-8.
6. Lai S, Zhou H, Xiong W, Gilbert M, Huang Z, Yu J, Yin W, Wang L, Chen Q, Li Y, Mu D. Changing epidemiology of human brucellosis, China, 1955–2014. Emerging infectious diseases. 2017 Feb;23(2):184.
7. Minas M, Minas A, Gourgulianis K, Stournara A. Epidemiological and clinical aspects of human brucellosis in central Greece. Jpn J Infect Dis. 2007;60:362-6.
8. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos E. The new global map of human brucellosis. Lancet Infect Dis. 2006;6:91-9.
9. Moradi Q, Canaani S, Pour MSM, Ghaderi E. Epidemiological study on 3880 patients with brucellosis in Kurdistan. Iran J Infect Trop Dis. 2006;11:27-33.
10. Mostafavi A, Asmand M. Trend of brucellosis (malt fever) in Iran, 1991-2008 (Persian). J Iranian Epidemiol. 2012;8(1):94-101.
11. Hotez, P.J., Savioli, L. and 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., vol.6, no. 2, p. e1475.
12. Soleimani A, Alizadeh S, Farshad MS, Kusha A, Mohamdzadeh M, Haghiri L, Zemestani A, Hoseini H. Descriptive epidemiology of human brucellosis in east Azerbaijan, 2001-2009. Medical Journal of Tabriz University of Medical Sciences and Health Services. 2012 Jun 12;34(1):63-9.
13. Mohammadian M, Mohammadian HA. Epidemiological characteristics and incidence rate of brucellosis over a period of 14 years in the Tiran-Karvan Township, Isfahan, Iran. (2014): 1-7.
14. Cromley EK. GIS and disease. Annual review of public health. 2003 May;24(1):7-24.
15. Nykiforuk CI, Flaman LM. Geographic information systems (GIS) for health promotion and public health: a review. Health promotion practice. 2011 Jan;12(1):63-73.
16. Hamzavi Y, Khademi N, Ghazizade MM, Jahanbakhsh A. Epidemiological study of brucellosis in Kermanshah province in 2011. J Kermanshah Univ Medi Sci 2011; 18:114-21.
17. Donev D, Karadzovski Z, Kasapinov B, Lazarevik V. Epidemiological and public health aspects of brucellosis in the Republic of Macedonia. Prilozi 2010; 31:33-54.
18. Zeinalian Dastjerdi M, Fadaei Nobari R, Ramazanpour J. Epidemiological features of human brucellosis in central Iran, 2006-2011. Public Health. 2012;126(12):1058-62.
19. Mustafa Kasim Karahocagi MK, Irmak H, Baran Al, Karsen H, Evirgen O, Akdeniz H. Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. Inter J Infect Dis. 2010;14(6):469-78.
20. Sofian M, Aghakhani A, Velayati A, Banifazl M, Eslamifar A, Ramezani A. Risk factors for human brucellosis in Iran: a case control study. Int J Infect Dis. 2007;12:157-61.

21. Eldeib A, Shallik N, Elrashidy A, Elsheikh H, Zaki M, Abdou S. Brucellosis trend and effect of domestic livestock vaccination on disease incidence in human. Tanta Med Sc J. 2008;3:7-18.

22. Shirima G, Fitzpatrick J, Kunda J, Mfinanga G, Kazwala R, Kambarage D. The role of livestock keeping in human brucellosis trends in livestock keeping communities in Tanzania. Tanzania J Health Res. 2010;12:203-7.

23. Pakzad, R., Pakzad, I., Safiri, S., Shirzadi, M.R., Mohammadpour, M., Behroozi, A., Sullman, M.J. and Janati, A. (2018). “Spatiotemporal analysis of brucellosis incidence in Iran from 2011 to 2014 using GIS,” Elsevier.

24. Li YJ, Li XL, Liang S, Fang LQ, Cao WC. Epidemiological features and risk factors associated with the spatial and temporal distribution of human brucellosis in China. BMC Infectious Diseases. 2013 Dec;13(1):1-2.

25. Abdullayev R, Kracalik I, Ismayilova R, Ustun N, Talibzade A, Blackburn JK. Analyzing the spatial and temporal distribution of human brucellosis in Azerbaijan (1995-2009) using spatial and spatio-temporal statistics. BMC Infectious Diseases. 2012 Dec;12(1):1-2.

Figures
Figure 1

Study area and Brucellosis frequency of Ardabil province, Northwest of Iran. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.
Figure 2

The monthly frequency of Brucellosis cases in Ardabil province, Northwest of Iran.

Figure 3

The trend of brucellosis in Ardabil province, Northwest of Iran.
Trend and IDW results of brucellosis diseases in Ardabil province, Northwest of Iran. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

**Figure 4**

Moran’s I autocorrelation and General G factor analysis of Brucellosis cases in different counties of, Northwest of Iran.