

Determination of High Risk Regions of Human Brucellosis in Turkey Using Exploratory Spatial Analysis

Türkiye’de İnsan Brusellozu için Riskli Bölgelerin Keşifçi Mekansal Analiz Yöntemleri Kullanılarak Belirlenmesi

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ABSTRACT Objective: Human brucellosis, still the most common bacterial zoonosis worldwide, is a notifiable disease in many countries, including Turkey. A tremendous growth of brucellosis has been observed in the last decades. Therefore, we aimed to explore the presence of regional clustering of brucellosis in Turkey, using explorative spatial analyses. **Material and Methods:** The recorded human brucellosis cases (1975-2006) by the Turkish Ministry of Health, the numbers of farm animals from 1996 to 2006 and demographic data from the Turkish Statistical Institute were used for analyses. Spatial analyses, including local and global spatial autocorrelation methods were performed for the brucellosis cases (1996-2006), to detect any trend or cluster and relationship with animal numbers for any particular province. **Results:** Global spatial autocorrelation indices indicated significant clustering of brucellosis (Moran’s I: 0.117 p= 0.005, Geary’s C: 0.86 p= 0.005). Spatial analyses of 147 391 brucellosis cases showed a trend towards to the southeast region of Turkey and clustering in 6 provinces in common and totally 9 provinces by two different methods (p< 0.05). Additionally, a relationship was detected between brucellosis and higher animal numbers (p< 0.05). **Conclusion:** This study shows that human brucellosis is a serious public health concern in the southeast region of Turkey and that region should have a priority to implement precautionary measures. It also shows that spatial analyses and statistics can contribute to the understanding of the epidemiology of diseases and identifying high rate disease locations. Besides, we suggest that underlying risk factors should be investigated further particularly where the cluster is observed.

Key Words: Brucellosis; epidemiology; geographic information systems; Turkey

ÖZET Amaç: İnsan brusellozu Türkiye’nin de dahil olduğu birçok ülkede hâlâ dünya çapında en yaygın ve bildirimi zorunlu zoonotik hastalıklardandır. Son yıllarda Türkiye’de bruselloz olgularında önemli bir artış olduğu gözlenmiştir. Bu çalışmada keşifçi mekansal analiz yöntemleri kullanılarak, Türkiye’de bruselloza ait bölgesel bir kümelenmenin olup olmadığının belirlenmesi amaçlanmıştır. **Gereç ve Yöntemler:** Çalışmanın analizlerinde T.C. Sağlık Bakanlığının 1975-2006 yılları arasındaki kayıtlı insan bruselloz olgularına ait veriler, 1996-2006 yıllarına ait Türkiye İstatistik Kurumunun hayvancılık ve demografik verileri kullanılmıştır. Bu verilerin 1996-2006 yıllarına ait olanları lokal ve global mekansal otokorelasyon yöntemleri uygulanarak, illerde bruselloz olgularında bir trend veya kümelenme olup-olmadığı ve hayvan sayıları ile insan bruselloz olguları arasında bir ilişki olup olmadığı analiz edilmiştir. **Bulgular:** Global mekansal otokorelasyon indeksleri bruselloza ait istatistiksel açıdan anlamlı olarak bir kümelenmenin varlığına işaret etmiştir (Moran’s I: 0.117 p= 0.005, Geary’s C: 0.86 p= 0.005). Toplam 147.391 bruselloz olgusunun mekansal analizleri Türkiye’nin güneydoğusuna doğru bir trend ve iki farklı yöntem ile de 6 ilde (toplam 9 ilde) bruselloz olgularında bir kümelenme olduğu saptanmıştır (p< 0.05). Ayrıca, hayvan sayılarının yüksek olduğu yerler ile bruselloz olguları arasında ilişki olduğu belirlenmiştir (p< 0.05). **Sonuç:** Bu çalışma, insan brusellozunun özellikle Türkiye’nin güneydoğusu için sıklık açısından önemli bir halk sağlığı sorunu olduğunu, dolayısıyla hastalığın önlenmesinde koruyucu önlemlerin alınması için öncelikli bölge olması gerektiğini göstermektedir. Bu çalışma aynı zamanda mekansal analiz ve istatistiksel yöntemlerinin hastalık hızının yüksek olduğu yerleri belirlemede olduğu kadar, hastalıkların epidemiyolojisini anlamaya katkıda bulunabileceğini de göstermektedir. Ayrıca, bu verilerin doğrultusunda, özellikle kümelenmenin olduğu yerlerdeki risk faktörlerinin ileri araştırılmasının yapılması uygun olacaktır.

Anahtar Kelimeler: Bruselloz; epidemiyoloji; coğrafi bilgi sistemi; Türkiye

Brucellosis is a typical zoonotic infection of domestic and wild animals caused by organisms in the genus *Brucella*.¹ The disease is transmitted to humans by animals through direct contact with infected materials or indirectly by ingestion of animal products and by inhalation of airborne agents. In humans, especially in developing countries, intake of raw milk and raw milk products such as cheese (particularly fresh cheese) is the major source of infection; however, other factors such as methods of food preparation, heat treatment of dairy products and direct contact with animals also influence the brucellosis risk for the population.^{2,3}

Brucellosis exists worldwide and is a notifiable disease in most countries, including Turkey. Human brucellosis is still the most common zoonotic disease throughout the world with more than 500.000 annual new cases.^{2,4} It still remains endemic as well as under-diagnosed and under-reported in some developing countries, possibly due to the low levels of surveillance and reporting.^{5,6} Human brucellosis has serious public health consequences in endemic areas and in Turkey it has important clinical consequences.^{5,7} This disease is considered endemic in Italy, Greece, Macedonia, Yugoslavia, Turkey, Lebanon, India, Middle and South America, whereas, it is eradicated in England, Nordic Countries, Australia, New Zealand and Canada. The situation in certain countries of the Middle East (such as Syria) is rapidly worsening.^{1,3,4,8-10} Nevertheless, the true incidence of human brucellosis is unknown.²

Turkey is also among the countries where brucellosis is endemic and *Brucella melitensis* is more common.² In terms of genetic factors predisposing to human brucellosis in Turkey, several gene polymorphisms (basically, cytokine gene polymorphisms) were also investigated and some genotypes of IL-10 and IL-6 were suggested to be risk factors for developing the disease.¹¹

Disease maps are useful tools for many aims, i.e. identification of areas of the true underlying geographical distribution of the disease incidence, assisting in the formulation of hypotheses about

disease etiology and assessing potential needs for geographical variation in follow-up studies.¹² The development of information system technology over the last 30 years has provided a powerful tool to examine spatial patterns; therefore, Geographical Information Systems (GIS) have had place in public health and epidemiologic researches.¹³ With the rapid development and adaptation of GIS technology for visualizing, managing, exploring and analyzing spatial data, spatial statistics and spatial analysis methods included in GIS software modules, started to receive increasing attention.

Brucellosis is considered to show different distributions and clustering patterns due to the geographical, economical, environmental and cultural differences among the provinces of Turkey.

This study, aimed to generate informative risk maps of human brucellosis in Turkey using health data and to identify infection cluster areas to improve the quality of the brucellosis control program. Another goal of the study was to explore whether the increase in the number of brucellosis cases was associated with the population size and/or distribution of livestock, by linking brucellosis data of human and animals for each province.

MATERIAL AND METHODS

Study Area

Turkey is both a European and Middle Eastern country, which is surrounded by Bulgaria at the northwest, Georgia at the northeast, Armenia and Iran at the east, and Syria and Iraq at the south. There are seven major geographical regions in the country as follows: Marmara, Aegean, Mediterranean, Central Anatolian, Black Sea, Eastern and Southeastern Anatolian regions. It is generally known that Eastern and Southeastern Anatolian regions are socioeconomically less developed regions than the other ones. Moreover, there are 81 provinces in these seven regions in Turkey.

Brucellosis Databases

All data regarding the total number of brucellosis cases recorded in Turkey between the years 1976-2006 were obtained from the Ministry of Health of Turkey. The data regarding the distribution of bru-

cellosis cases to provinces in Turkey, between the years 1996-2006 were also obtained from the Ministry of Health of Turkey; provincial records for the years 1976-1995 were not available. Thus, the data of the years 1996 to 2006 were used for spatial analyses.¹⁴ Populations by census year, annual intercensal rate of increase, mid-year population forecast data and total numbers of farm animals (including cattle, sheep and goats) in these provinces were obtained from the Turkish Statistical Institute.^{15,16}

Statistical Methods and Calculations

For Spatial Analysis, three different software programs were used for visualization of the health and animals data. These were as follows: Arc GIS 9.2 developed by ESRI, GeoDa 0.9.5-I developed by Luc Anselin through the Center for Spatially Integrated Social Science at the University of Illinois, and Crime Stat 3.1 developed by Ned Levine with support from the National Institute of Justice.¹⁷

Aggregated area-based data are very important sources of information for many science disciplines. Geographical locations of these data are also important factors in many areas of social, science and economic policies at the national level because demographical, geographical, social and economic characteristics of the society that represent aggregated province units show differences throughout the country. Province is a common unit for social, economic, demographic and administrative data collection by agencies in Turkey. Health and animal data were examined with spatial analyses at the province level in this study. Usage of provinces in analyses allowed comparing health data with other demographical and animal data. However, using province units have important limitations; provinces are administrative units and cover large areas with different heterogeneous populations. Besides, they may not match the ecological scale at which diffusion processes for brucellosis.¹⁸ Consequently, it is thought that aggregating the brucellosis rates for the entire eleven years provides the advantage of stability in the province-level disease rates and it summarizes the phenomenon.

Since the brucellosis data were aggregated into the areal units of provinces, an important aspect was deriving spatial weight matrix (W) for spatial analyses. W is the fundamental tool used to model the spatial proximity and interdependence between areal units. Determination of the proper W matrix is a difficult and controversial topic in spatial analyses.^{19,20} In this study, three different W matrices were formed for the spatial analyses. The first and second matrices were formed based on the criterion of contiguity according to the centroids of nearest 6-12 neighbors. The third matrix was formed according to the criterion of inverse distance.

Using the midyear population and the number of cases, incidence rates were calculated for the 1996-2006 period for studying distribution of brucellosis by provinces. While working with aggregated data, if the population or the number of cases is relatively small and sparse, rate estimates may not be precise. In order to overcome the problem of rate instability, various smoothing methods are mostly implemented.¹⁷ The idea in smoothing is to borrow the information from other small areas for the estimation of the relative risk. The information can be borrowed either from nearest areas (local smoothing) or from all areas in the study area (global smoothing). There are a number of techniques for smoothing data, such as mean or median based techniques, either weighted or unweighted and empirical Bayes techniques.²⁰

In this study, Empirical Bayes (EB) smoothing was used and raw incidence rates were replaced with their globally smoothed values calculated by EB tool in ArcGIS 9.2 created by the National Cancer Institute of USA.

Spatial analysis techniques used with areal data are usually based on data aggregated for administrative units of observation. The main emphasis with areal data is on detection and explanation of spatial patterns and trends.²¹ Therefore, after rate smoothing was performed, a spatial rate smoother based on the notion of a spatial moving average was carried out for explorative spatial data analysis. The purpose of integrating spatial rate smoother met-

hod was to emphasize global variations and trends in the health data. Spatial rate smoother does not compute an estimate as the raw rate for each area. Instead, it computes for that area together with a set of reference neighbors.²¹

To explore spatial dependence, showing how the incidence rates were correlated in the country, Moran's I and Geary's C values were calculated with three weight matrices. Moran's I and Geary's C use the magnitude of incidence rates to identify and measure the strength of spatial patterns.^{22,23} Moran's I value is produced by standardizing the spatial auto covariance by the variance of the data using a measure of the connectivity of the data, while Geary's C uses the sum of squared differences between pairs of data values as its measure of covariation. The range of possible values of Moran's I was taken -1 to 1, where positive values indicated spatial clustering of similar values and negative values indicated a clustering of dissimilar values. The possible values of C is ranged between 0 and 2, where a value of C close to 0 means the distribution of values clustered, conversely a value of C close to 2 means the distribution of values dispersed. For both Moran's I and Geary's C values statistical significance is calculated through a number of formulae that have been derived by either the normal approximation or by randomization experiments.

Since Moran's I and Geary's C methods indicate clustering of "high" or "low" values, and these methods can not distinguish between these situations, general G statistics was used to understand clustering of high or low values, and to show either hot or cold spots which exist in the region.

These global spatial data analysis show clustering but they do not show where the clusters are. To investigate the spatial variation as well as the spatial associations, it is possible to calculate local versions of Moran's I (LISA), Geary's C, and the General G statistics for each areal unit in the data. Local indicators produce a specific value for each area allowing the identification of where the clusters are. Local Moran's I and G_i^* statistics of Getis and Ord methods were used to explore whe-

re the diseases were clustered.^{22,23} Local Moran's I was used as a local indicator of spatial association which investigates clusters of areas with similar values and those with different values. A high value of I means that the area is surrounded by features with similarly high or low values while a low value of I means that the area is surrounded by features with dissimilar values. Local analyses based on the LISA statistics were visualized in the form of significance and cluster maps. In addition, G_i^* statistics was used to detect local pockets of dependence that may not show up by using global spatial autocorrelation methods, suggested by Getis and Ord.^{23,24} The G_i^* statistic is often used to identify whether high values (hot spots) or low values (cold spots) exist based on distance. A high value of G_i^* statistic indicates a spatial cluster of high values, where a low value of G_i^* statistic indicates a spatial cluster of low values around the area.

After the determination of clusters, to increase confidence in interpreting spatial patterns in the relation between brucellosis and the distribution of the animals, the relation between brucellosis rates and the number of animals in provinces were further explored, using multivariate spatial autocorrelation. This statistics shows the correlation between one variable at a location and a different variable at the neighboring locations. Greater similarity that indicated under spatial randomness implies spatially similar clusters in the two variables, while greater dissimilarity implies negative relationship between the two variables.²⁵ The resulting multivariate LISA cluster map shows significant locations classified by the association between the animal value at one province with brucellosis rate and the value for its neighbors, suggesting possible diffusion patterns. The high-high and low-low locations suggest significant clustering of similar values, whereas the high-low and low-high locations indicate spatial outliers. It is important to keep in mind that these exploratory techniques are only suggestive of possible hypotheses and relations. Confirmation of such patterns belongs to the domain of spatial modeling, which is outside the scope of this paper.

RESULTS

We analyzed a total of 200 465 recorded brucellosis cases from the Ministry of Health database for the period of 1975-2006 as well as 147 391 cases for the period of 1996-2006.¹⁴ The nationwide morbidity values (per 100.000) for the period of 1975-2006 were shown in Figure 1. Clearly, an increase in the morbidity of brucellosis can be seen; about 5 in 1990s, over 15 in 2000 and about 25 in 2005 per 100,000.

Analysis of the number of brucellosis cases based on provincial distribution including the smoothed incidence rates of brucellosis (1:100.000) using EB method for the period of 1996-2006 were shown in Figure 2.

Aksaray, Siirt, Bitlis, Batman, Şırnak, Hakkari and Diyarbakır were determined as the upper outlier cities with 3.0 interquartile extreme rates for brucellosis, based on the results of descriptive box plot analyses which are useful for describing the general characteristics of the distribution of brucellosis and for revealing specific provinces with high levels of disease.

However, they are limited to identify any significant spatial clustering of brucellosis rates. Altogether, these rates of incidence show that there seems to be a trend towards the South and Eastern Anatolian regions for the cases of human brucellosis.

To assess if there was significant clustering in Turkey in terms of brucellosis cases we did analyses using global spatial autocorrelation methods (Table 1). Moran's I values for all three-weight matrices were positive and higher than the expected index value. In addition, General G showed a higher value than expected and Geary's C value indicated a value smaller than 1. Altogether all three analyses showed clustering, at 0.05 level of significance, throughout the country in terms of brucellosis cases in Turkey. Besides, the spatial rate method was used to emphasize global variations and trends in the data, which revealed that there was a clear trend towards southeast (Figure 3).

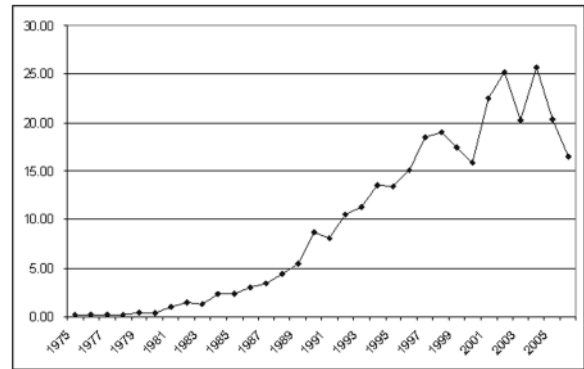


FIGURE 1: The morbidity values (per 100.000) of brucellosis in Turkey for the 1975-2006 period.

Finally, using local methods, location of clusters were investigated. Local auto correlation values with G_i^* statistics and clusters for brucellosis determined using LISA are shown in Figure 4. The Legend in figure 4 shows the results obtained from the first method (G_i^* statistical values; dark brown: $p < 0.05$) and the provinces of Diyarbakır, Mardin, Şırnak, Siirt, Batman, Bitlis, Muş, Van, Hakkari were determined as significant clusters, colored in dark brown. The selected objects with turquoise color shows the significant provinces determined as cluster with the LISA, which includes the provinces of Diyarbakır, Mardin, Şırnak, Siirt, Bitlis and Van. Overall, six provinces (Diyarbakır, Mardin, Şırnak, Siirt, Bitlis, Van) were detected with both methods used showing the clusters mainly in the southeast region.

The relationship between the clustering of brucellosis and the number of farm animals were further analyzed for provinces, using Multivariate LISA method. For this, the data were obtained from the Turkish Statistical Institute. The total numbers of farm animals (including cattle, sheep, goats) in the provinces for the years 1996 to 2006 have shown a decrease from 54.946.000 to 41.948.570 over eleven years.¹⁶ Figure 5A shows the spatial distribution of the total number of farm animals for provinces in Turkey for the 1996-2006 period. Obviously, the animal husbandry is more concentrated on the eastern and southeastern Anatolian regions, while it seems less in the other regions. As

TABLE 1: Global Spatial Autocorrelation values of brucellosis (NN: Nearest neighbor).

Diseases	Moran's I (W with Arc GIS)	Expected Index	Z Score	Moran's I (12 NN W with GeoDa)	P Value	Moran's I (6 NN W with GeoDa)	P Value	Observed G	Expected	Z Score	Geary's C	Z Score
Brucellosis	0.117	-0.013	8.5	0.252	0.005	0.389	0.005	0.346	0.255	5.46	0.86	-5.0

can be seen in Figure 5B, the number of animals and human brucellosis cases are high in the southeastern region of Turkey. Multivariate LISA analysis results showed that there was a relations-

hip between the number of farm animals and the cases of human brucellosis, that is, as the number of animals increase the number of human brucellosis cases increase.



FIGURE 2: Choropleth maps of smoothed rates of brucellosis (1:100.000) according to the provinces of Turkey for the 1996-2006 period.



FIGURE 3: Choropleth Map of spatial rate smoother values with Geo Da.



FIGURE 4: Choropleth Map of Local auto correlation values with G_i^* statistics and clusters with LISA.



FIGURE 5A: The number of total farm animals (cattle, sheep, goats) distribution (1:1.000) for the provinces of Turkey for the 1996-2006 period.

DISCUSSION

Recently, many epidemiologists have aimed to develop spatially distributed process models for different diseases. The spatial models might link the disease location, environment, transmission function, space and time. In addition, the process understanding encapsulated by the models might allow predictions to be made for the future. These are based on (a) real-time scenarios (i.e. using data assi-

milation techniques) for early warning, preventing and controlling or training for the disease efficiently and (b) possible “what-if” scenarios of the future (i.e., under uncertain climate change).²⁶

Spatial analysis method has been used for many purposes such as detection of candidate loci for selection in the area of genomics.²⁷ It was introduced as a new method to detect signatures of natural selection based on the application of spatial analysis, with the contribution of GIS, environ-



FIGURE 5B: Multivariate LISA cluster map of number of farm animals against brucellosis rate.

mental variables and molecular data. In a study conducted in Iran, GIS applications were used to explain spatial distribution of brucellosis in an endemic district in a brucellosis control programme.²⁸ This study showed that GIS applications could generate informative risk maps of brucellosis using health and veterinary data, which may improve the quality of the control program. Moreover, this study supports the findings of our study, that is, human brucellosis is associated with population size and distribution of cattle in rural areas. In addition, spatial epidemiological investigations are often exploratory with limited information about the putative risk factors. Indeed, it is often the primary motivation for the analysis to identify unknown geographically varying risk factors. This exploratory approach to relative risk mapping gives the investigator an impression about the importance and geographical distribution of the unknown spatial risk factors.²⁹

In the present study, spatial analysis and spatial statistics were demonstrated as applicable methods to study the distribution of human brucellosis. Furthermore, this study constitutes the first report on spatial analyses of human brucellosis in Turkey. The distributions of human brucellosis reports for the period of 1996-2006 were mapped and significant clusters were identified using two spatial clus-

tering methods. Each cluster had a high rate of brucellosis reports after smoothing. The smoothed data provides more accurate visual representation of the overall distribution of the standardized rates compared to the original map of observed incidence rates, whereas the cluster analysis pinpoints statistically significant geographical areas generating reports of human brucellosis.

Human brucellosis is still a public health problem, partly because of the expansion of animal industries and urbanization and lack of hygienic measures in animal husbandry and in food handling.³⁰ The epidemiology of human brucellosis was evolved, reflecting alterations in socioeconomic parameters, improvements in recognition and notification systems, outcomes of ongoing eradication programs of animal brucellosis and the evolution of the “global village” through international tourism.⁴ While the disease was eradicated in England, North European countries, Australia, New Zealand and Canada, the situation remains serious in many developing countries (i.e. Syria in Middle East).^{3,4,8-10} On the other hand, it is still endemic in certain Mediterranean countries such as Italy, Lebanon, Greece, Turkey, as well as India, Middle and South America.⁸ The reported prevalence of brucellosis in rural areas is high in some Middle East countries like Saudi Arabia, Iran, Kuwait, Lebanon and Jordan.³¹

In Turkey, the number of reported cases increased from 69 to 18,264 in the last thirty years.¹⁴ Although the number of animals in the last eleven years (1996-2006) shows a decrease, the number of human brucellosis cases show a steady increase for the recent years, particularly after 1990.¹⁶ Given the improvements in diagnostic facilities and reporting system in the very recent period, it might reflect the underdiagnosis of the human brucellosis cases in the very early years. In a multi-center study between 1984 and 1987, seropositivity was 1.8% in the normal population and 6.0% in the high risk population, whereas in other studies the seropositivity ranged from 2.2% to 3.4% in comparison to the higher prevalence found among people dealing with livestock and consuming raw milk and milk products.³²⁻³⁴ Çetinkaya et al also found that the prevalence of brucellosis decreased as educational levels increased.³⁴ They also reported that seropositivity rate was especially high in people who had a family history of brucellosis suggesting the involvement of certain environmental factors such as some possible socioeconomic risk factors, for example sharing of family meals resulting in family clusters of infection, as well as possible genetic factors. In the present study, using two methods, the disease was found to be clustered in the Southeast Region (provinces of Diyarbakır, Mardin, Siirt, Bitlis, Şırnak and Van). Our data are in agreement with the previous reports suggesting clustering of brucellosis cases in the region where general urbanization is not very high and the education levels are lower than the Turkey's average, as well as poor hygienic conditions and some unhealthy nutritional habits such as, the consumption of raw milk products and fresh cheese. Therefore, determination of high-risk zones for human brucellosis would be useful to establish education programs, particularly for the high-risk families and to allocate funding for public health.³⁵ Understanding the risk factors and sources of infection and the clustering of human brucellosis in time and space might have important public health implications.³⁶

We also analyzed the possible relationship between this clustering and the number of animals in those regions. It turned out that a highly signifi-

cant association was present with the number of animals in the region where clustering was found earlier. Furthermore, non-clustering in other regions in our study is compatible with the data for animal numbers in this region supporting that association as well. However, it is difficult to estimate the underlying mechanism and how it is reflected in the human brucellosis cases. One possibility could be attributed to the two transmission routes (occupational or food-borne) taking part in the human disease incidence in rural area, as both could be deeply related to the size of the local animal population as suggested before.²⁸ For better conclusion, further investigation on other possible risk factors, e.g. disease prevalence of animal population, livestock vaccination coverage and local customs would give some new evidence of local animal population association with epidemiology of human disease.²⁸

Genetic factors also appear to have a role in the pathogenesis of human brucellosis. The impact of several polymorphisms on brucellosis and their possible relationship with disease progression has been investigated and several alleles or genotypes of the genes were found to be more prevalent in patients with brucellosis compared to healthy controls in different populations showing or suggesting a possible association with the predisposition or resistance to human brucellosis.^{11,37-42} However, in order to confirm the biological significance of the results, further studies were suggested to be performed in larger population sizes.¹¹ On the other hand, there seems to be no report investigating if there is a regional discrepancy for genetic factors predisposing to human brucellosis. Therefore, our data showing a clustering of brucellosis cases in the southeast region suggests that the underlying environmental and genetic factors making people susceptible to brucellosis in this particular region needs to be further analyzed.

One of the limitations of our study was the lack of national data on animal brucellosis rates in Turkey. This data would be helpful for understanding the real situation of transmission routes of brucellosis in Turkey. Second, determining the risky and the lower-risk areas and the transmission

routes and investigation of spatial clustering of the diseases over the years simultaneously is important. However, there are some difficulties to conduct these methods in our country such as monitoring the residencies of the human cases in order to carry out an individual or family based cluster analysis. As a result, that would make it difficult to get more and exact information on people at risk. Third, while using spatial analysis methods it would be better to obtain the multiple data on risk factors as well as confounding factors such as the individuals' age, gender, and income status and involvement with husbandry, which are impossible to reach in other ways simultaneously to benefit from time and labor efficiently.

In addition, since this study is an ecologic one it should not be disregarded that ecologic fallacy is always a possibility for these findings and associations. Similarly, because it is not possible to use the ecologic data for individual risk calculation,

further analytical studies are needed to confirm them.

CONCLUSION

Spatial analyses and statistics significantly contribute to the understanding of the epidemiology of diseases. With the aid of these analyses, it will be effective to monitor and identify high rate disease locations or regions and to implement precautionary measures and provisions. This study showed that human brucellosis cases clustered particularly in the southeastern region of Turkey. Accordingly, it seems a major public health problem in this region based on the high frequency of disease rates and therefore, this region should be regarded as a region of priority to take precautions for the prevention of the disease. Further studies are needed to investigate environmental factors as well as genetic factors to effectively control and eradicate brucellosis in this region.

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