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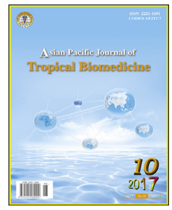

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Spatiotemporal clustering of cutaneous leishmaniasis in Fars province, Iran

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ABSTRACT

Objective: To assess the spatiotemporal trait of cutaneous leishmaniasis (CL) in Fars province, Iran.
Methods: Spatiotemporal cluster analysis was conducted retrospectively to find spatio-temporal clusters of CL cases. Time-series data were recorded from 29 201 cases in Fars province, Iran from 2010 to 2015, which were used to verify if the cases were distributed randomly over time and place. Then, subgroup analysis was applied to find significant sub-clusters within large clusters. Spatiotemporal permutation scans statistics in addition to subgroup analysis were implemented using SaTScan software.
Results: This study resulted in statistically significant spatiotemporal clusters of CL ($P < 0.05$). The most likely cluster contained 350 cases from 1 July 2010 to 30 November 2010. Besides, 5 secondary clusters were detected in different periods of time. Finally, statistically significant sub-clusters were found within the three large clusters ($P < 0.05$).
Conclusions: Transmission of CL followed spatiotemporal pattern in Fars province, Iran. This can have an important effect on future studies on prediction and prevention of CL.

1. Introduction

Leishmaniasis is the second most noticeable vector-borne protozoa disease after malaria regarding both number of affected people and fatality. It is a parasitic infectious disease caused by species of genus *Leishmania* transferred by infected phebotomine sand fly bites. There are four main types of leishmaniasis, namely anthroponotic and zoonotic visceral leishmaniasis (VL) and anthroponotic and zoonotic cutaneous leishmaniasis (CL). Humans are supposed to be the only source of infection for sand fly vectors in anthroponotic types. In zoonotic types, animals are reservoirs that maintain and spread *Leishmania* parasites. The cutaneous type of *Leishmania* usually causes skin ulcers on open parts of body. It may bring about a great number of ulcers ending up in harsh disabilities and generate lasting ulcers, which can be a social stigma. The severity of medical pathology depends on parasitic species, species of the involved vector, and geographical site [1–8]. Since CL is associated with open-air activities, such as cultivation, mining, deforestation, and road building, it can be considered to be an earth-based phenomenon.

Involvement of humans with the vector's life cycle can induce a great risk of infection. In addition, vegetation density, poor sanitation, construction derbies, and building ruins have created an appropriate situation for sand flies to live and reproduce, which can help the disease to be transmitted faster [8]. Generally, more than 350 million people are at risk of leishmaniasis in 88 countries around the world and nearly 12 million people are currently contaminated. Indeed, approximately 2 million new cases occur yearly among which 500 000 cases are visceral leishmaniasis and the other 1 500 000 ones are CL. Moreover, nearly 90 percent of CL cases are located in Afghanistan, Algeria, Brazil, Iran, Peru, and Saudi [9–11].

CL is heavily correlated to poverty, and a large portion of efforts have been devoted to controlling the sources and reservoirs of infection. CL is the representative of highly-prevalent diseases in Fars province, Iran that is known to be an endemic [7]. Sand flies live in a large zone of Fars province, including Sepidan, Arsenjan, Neireez, and Estahban cities. In the last

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year, almost 6 000 cases were reported in Fars province among which 2 000 cases occurred in urban and 4 000 ones in rural areas. The incidence rate of CL has been reported to be 106.01–144.00 cases per 100 000 inhabitants. Increase in the number of CL cases in the recent years can be partially due to an increase in poverty and lack of proper sanitation. In the capital of Fars province, Shiraz, the number of cases increased from 765 in 2012 to 1 386 in 2012 [7]. The same increasing pattern has also been observed in almost all cities of the province.

Investigation of features of CL can be used to improve disease management, including prediction and prevention. The spatial and temporal pattern of CL transmission has not been considered in Fars province yet. Therefore, it should be regarded as a problem of time and place simultaneously. Spatiotemporal statistical analysis used to detect significant clusters helps hypothesize the relations between CL and place and time. To make the best decision on public health costs and supervision, CL patterns as well as environmental factors (like time and space) need to be taken into account. In this framework, spatiotemporal statistical analysis of CL process that aims to find clusters (nonhomogeneities) offers very beneficial knowledge for CL prediction and prevention planning and ultimately public health promotion. There are several methods of detecting clusters considering just time or space features of CL [7,12,13]. However, scan statistic regards both temporal and spatial features of CL simultaneously, which is most profitable. In a previous study, the results of spatiotemporal statistical analysis indicated that transmission of American cutaneous leishmaniasis followed a spatiotemporal pattern in Venezuela, USA [8].

Health status changes in different geographical locations as well as different time periods. Thus, it is crucial to specify these differences and detect areas with an accumulation of health problems, which is of particular importance regarding epidemiological and public health viewpoints. Modern technologies, such as Geographic Information System and SaTScan, with help of scan statistics have enabled us to do disease mapping and spatiotemporal clustering in epidemiological researches.

The current study aims to evaluate spatiotemporal characteristics of CL in Fars province as an endemic area and to determine spatiotemporal clusters in this province from 2010 to 2015.

2. Materials and methods

2.1. Study design

Time-series design, including 29 201 incidence cases of CL recorded in Fars province from 2010 to 2015, was conducted retrospectively to verify if the cases were distributed randomly over time and space. To investigate the spatiotemporal features of CL, spatiotemporal permutation scan statistics was used.

2.2. Study area

Fars province, with Shiraz as its capital city, locates in the south of Iran, covering an area of 122 661 km^2 (7% of the total area of the country). Geographically, Fars province is located on 27°3′ and 31°40′ northern latitude and 50°36′ and 55°35′ western longitude. This province is composed of 26 cities, and geographical coordinates of each city were found through Google-Earth (US Department of State Geographer 2016). The province has three disparate atmospheric regions the first of which being the mountainous sites of north and northwest with mild chill winters and moderate summers. The second part includes central regions with rather rainy winters and hot dry summers. Finally, the third region is located in south and southeast with cold winters and hot summers. The average temperature of Shiraz is 16.8 °C ranging from 4.7 °C to 29.2 °C. Besides, its average altitude is 5 000 feet above the sea level. Based on 2011 census, the population of Fars province is 4.6 million people (6% of the total population of Iran), including 67.6% urban dwellers (urban areas and suburbs), 31% villagers (small towns and rural areas), and 0.3% nomad tribes. The current population growth rate was reported to be 1.3 percent in 2015. It should also be noted that there are migratory movements between the capital of the province and other cities [1].

2.3. Subjects

This study was performed on 29 201 confirmed CL cases. The cases were patients from 26 different cities of Fars province registered in the Contagious Disease Control center located in the main stance of School of Medicine, Shiraz, Iran. These cases showed positive CL through smear, culture, or polymerase chain reaction. Patients whose symptoms of CL began from 1 January 2010 to 31 December 2015 were included.

2.4. Population data

Clinical diagnosis of CL was obtained from the patient's medical records. Cases were recorded monthly from 1 January 2010 to 31 December 2015 for each city. Additionally, all cases recorded in each city were summed up to count the number of cases in that city. The geographical coordinates for each city were obtained through Google-Earth based on latitude–longitude coordinate system. Finally, the data were stored in Microsoft Excel 2007 and were exported to text format for further analysis.

2.5. Information processing

SPSS, version 22 was used for statistical analysis and ITSM2002 software was employed for detecting the general trend of CL over time. In addition, maps of CL cases were generated in ArcGIS, version 10. Finally, SaTScan, version 9.4.4 was used for spatiotemporal cluster analysis.

2.6. Statistical analysis

Median ± quartile deviation was used for continuous variables and minimum, maximum, relative frequency, bar charts, and frequency distribution tables were applied for qualitative variables. To testify the normality assumption, Kolmogorov–Smirnov test was used. In addition, *Chi*-square test was utilized to assess the equal frequency of malaria occurrence over time and place. Kruskal–Wallis test was also used to evaluate the equality of median of cases through different time periods and places. Significance level was considered to be 0.05 for all statistical tests. It should be noted that moving average method was applied to explore the general trend of CL occurrence over time.