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Spatial modeling of cutaneous leishmaniasis in Iran from 1983 to 2013

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ABSTRACT

Introduction: Cutaneous Leshmaniasis (CL), a parasitic skin infection caused by *Leishmania* species, is endemic in some regions of Iran. In this study, the effect of location on the incidence and distribution of CL in Iran was studied.
Methods: We collected datas including the number of Cutaneous Leishmaniasis cases and populations at-risk of disease in Iran's different provinces reported by the Iranian ministry of health and the National Bureau of Statistics, respectively. Spatial modeling was performed using Arc GIS software. Descriptive maps, hotspot analysis, and high/low clustering analysis were used to demonstrate distribution of the cutaneous leishmaniasis, to determine regions at risk of disease's incidence, and to reach the most appropriate method for clustering of disease.
Results: The total number of cases of cutaneous leishmaniasis reported through the study period was 589,913. The annual incidence of CL was estimated to be 30.9 per 100,000 in Iranian population. We also demonstrated that Cutaneous leishmaniasis most prominently occurs in regions with dry and desert climates as well as in central parts of Iran. It affected the southwest of Iran between 1983 and 1997, and subsequently developed towards the center and the eastern between 1998 and 2013. Disease hotspots were focused in the provinces of Yazd, Khozestan and Kohgiloyeh-Boyer-Ahmad ($p < 0.05$). No pattern of spatial clustering was observed.
Conclusion: Cutaneous leishmaniasis is a major health problem which could be a serious threat for inhabitants who live in high-risk provinces of Iran; much more resources need to be allocated in these areas, to warrant the prevention as well as effectively management of this disease.

1. Introduction

Cutaneous leishmaniasis (Akhvlediani et al., 2010), a parasitic skin infection caused by a range of Leishmania species, is a public health problem affecting more than 60 countries located in tropical and subtropical regions worldwide (Desjeux, 2004). The total number of people affected is estimated to be 12 million. Between 2010 and 2015, 1 million newly infected cases of CL were reported (Leishmaniasis and facts, 2014; Shirzadi, 2012). In addition, approximately 90% of cases have been reported from Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia and Syria (Mirzazadeh et al., 2009). Victims infected often have lesions on their skin, without developing any other symptom (Anon, 2014a).

Being bitten by sandflies is the most common route of transmission for *leishmania*. Both types of CL have been reported in Iran, including *anthroponotic cutaneous leishmaniasis*, or ACL caused by *Leishmania tropica* and transmitted by *Phlebotomus* sergenty, and zoonotic cutaneous lieshmaniasis, or ZCL caused by Leishmania major and transmitted by *Phlebotomus papatasi* (Mohebali et al., 2004; Nadim et al., 2008).

CL is distributed unevenly among the provinces of Iran (Salahi-Moghaddam et al., 2015) and has imposed a significant adverse effect on the health system, as in 2008 alone, over 26,000 cases with an incidence of 37 per 100,000 were reported (Shirzadi, 2012; Akhoundi et al., 2013). There been various cities in Iran wherein CL has been developed, including: Bam (Mohebali, 2013; Chelbi et al., 2009), Mobarakeh, Natanz, Kashan, Ardestan (Gage et al., 2008; Kawa and Sabroza, 2002), Mehran and Dehloran (Raymond et al., 2003). Some studies have also introduced different carriers for leishmania in Iran such as: *Ph. papatasi, Ph. major, Ph. alexandri,*

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Ph. Sergenti and etc. (Nadim et al., 2008). There are also a couple of studies showing that some reservoirs of cutaneous leishmaniasis such as *R. opimus* and *M. libycus* are found more frequently in areas with high incidence of the CL Like: Mobarakeh, Natanz, Kashan and Ardestan in Isfahan province, Ardakan in Yazd province and Marvdasht and Niriz in Fars province (Mohebali et al., 2004; Nadim et al., 2008). Because of being vector borne and the fact that ZCL variant has non-human sources, certain weather conditions such as specific temperature, humidity and rain, are crucial factors in developing transmission (Mohebali, 2013). Moreover, some researches have declared that CL more frequently occurs in dry areas such as deserts (Chelbi et al., 2009; Gage et al., 2008).

Considering these circumstances, geographical factors, especially location, play a significant role in the incidence of CL both in human and animals. This effect has been evaluated using a Geographic Information System (Schröder, 2006). This system is capable of determining high-risk areas or "hotspots", as well as any non-random accumulation, or "clustering" of the disease. Additionally, several studies have utilized the GIS system to assess the distribution of leishmaniasis (Franke et al., 2002; Kawa and Sabroza, 2002; Raymond et al., 2003; Salomon et al., 2004). A study conducted in 2014 indicated a higher incidence in the rural plateaus of Iran (Salahi-Moghaddam et al., 2015). Similarly, there are couples of investigations on distribution of the CL in certain places such as deserts, plains, low-altitude, and high-density areas that have revealed the presence of a clustering pattern (Chelbi et al., 2009; Salomon et al., 2004; Balmaa et al., 1994; Ben-Ahmed et al., 2009; Demirel and Erdoğan, 2009; Rodríguez et al., 2013; Salah et al., 2007).

Given the extent of different foci and the geographical distribution in Iran, identification and examination of high-risk foci of CL and their time trends can be used as an effective tool to improve health services' quality. In addition, GIS has been efficiently served to accomplish this goal. To our knowledge, the distribution of CL (ACL and ZCL) by using GIS analysis has not yet thoroughly been studied in Iran. In this study, we examined reported data of CL incidence in Iran (between 1983 and 2013) and used a spatial model to identify high risk areas and also to look for evidence of disease clustering. The results will shed the lights for stakeholders to appropriately allocate resources targeting disease management and prevention in Iran.

2. Methods

2.1. The study area

Iran, a country in the Middle-East with the extent of 1,648,195 square-kilometers, has been ranked as the 18th largest country in the world with a population of over 75 million (2011) (Pappas et al., 2006). It has possessed a variety of environmental features such as a vast geographical length and breadth, topographic diversity, and an altitude up to 5671 m above sea level. The Iran's climate ranges from arid to subtropical, and the mean of rainfall varies from 100 to 2000 mm with a temperature ranging from 0 to 50 °C. Being surrounded by Armenia, Turkmenistan, and Azerbaijan at the north, (as well as by Russia and Kazakhstan via a water border in the Caspian Sea); Afghanistan and Pakistan at the East; the Persian Gulf and Gulf of Oman at the south; Iraq at the east; and Turkey at the northwest (Mostafavi et al., 2013), Iran has been currently divided into 31 provinces.

2.2. Reported incidence of CL

Reported data about the incidence of cutaneous leishmaniasis from the beginning of 1983 until the end of 2013 was collected at a provincial level. After cleaning and correcting of errors, information were entered into Excel datasheets. In situations where the only information was the number of cases reported, the incidence was calculated (Eq. (1)) by the extraction of populations at risk (total population of the province), reported by the National Bureau of Statistics.

$$\text{Incidence} = \frac{\text{Number of reported cases}}{\text{Total Population Risk}} 100,000 \quad (1)$$

Eq. (1): Incidence of cutaneous leishmaniasis.

2.3. GIS analysis

The most recently updated electronic map of Iran and its provinces was used and linked this map to excel file by join comment.

A choropleth map that uses a range of colors to show variable changes in the layers of polygons produced at the provincial level. A choropleth map of CL in time frames of 1, 5, 10, 15 and 31 years was created, for the reason of better detecting likely changes of distribution of CL.

Disease hotspots were identified by using the Getis-Ord Gi* statistic. The Hot Spot Analysis tool calculates the Getis-Ord Gi* statistic (Eq. (2)) for each province in a dataset. The resultant Gi score tells us how provinces with either high or low incidences spatially cluster. This tool works by analyzing each province within the context of neighboring provinces. A province with a high incidence of CL was considered to be a statistically significant Hot Spot especially when being surrounded by provinces with a high Incidence. The value belonged to a particular province was compared proportionally to that of the rest provinces; if the local value is much different than the expected local sum and difference is too large to be the result of random chance, a statistically significant Gi score would be obtained. To the contrary, a cold spot province is the one in which a low Incidence of CL is detected and also is surrounded by provinces with low Incidence (Anon, 2014b; Mahbubeh et al., 2014; Asgari, 2011).

$$G_i^* = \frac{\sum_{j=1}^{n} w_{i,j} x_j - \bar{X} \sum_{j=1}^{n} w_{i,j}}{S \sqrt{\frac{\left[n \sum_{j=1}^{n} w_{i,j}^2 - \left(\sum_{j=1}^{n} w_{i,j} \right)^2 \right]}{n-1}}} \quad (2)$$

Eq. (2): - Getis-Ord Gi* (Gi* Statistics) – where X_j is the Incidence of CL for province j, w_{ij} is the spatial weight between province i and j, n is equal to the total number of provinces.

$$G = \frac{\sum_{i=1}^{N} \sum_{j=1}^{N} w_{i,j} x_i x_j}{\sum_{i=1}^{N} \sum_{j=1}^{N} x_i x_j}, \forall j \neq i \quad (3)$$

Eq. (3): *G* statistics where x_i and x_j, respectively, are the Incidence of CL in the ith and jth Provinces; W_{ij} is the spatial weight between the Province *i* and *j*; *N* is the total Incidence of CL; and S_0 is the aggregate of all spatial weights.

For hot-spot analysis, spatial weight calculated by Fixed Distance Band method. In this method, each province is analyzed within the context of neighboring provinces. Neighboring provinces inside the specified critical distance receive a weight of one and exert influence on computations for the target province. Neighboring provinces outside the critical distance receive a weight