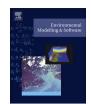
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### A spatially explicit agent-based modeling approach for the spread of Cutaneous Leishmaniasis disease in central Iran, Isfahan



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#### ABSTRACT

Cutaneous Leishmaniasis (CL) is an endemic vector-borne disease in the Middle East and a worldwide public health problem. The spread of CL is highly associated with the socio-ecological interactions of vectors, hosts and the environment. The heterogeneity of these interactions has hindered CL modeling for healthcare preventive measures in endemic areas. In this study, an agent-based model (ABM) is developed to simulate the dynamics of CL spread based on a Geographic Automata System (GAS). A Susceptible-Exposed-Infected-Recovered (SEIR) approach together with Bayesian modeling has been applied in the ABM to explore the spread of CL. The model is then adapted locally for Isfahan Province, an endemic area in central Iran. The results from the model indicate that desertification areas are the main origin of CL, and riverside population centers have the potential to host more sand fly exposures and should receive more preventive measures from healthcare authorities. The results also show that healthcare service accessibility prevented exposures from becoming infected and areas with new inhabitants experienced more infections from same amount of sand fly exposures.

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#### 1. Introduction

Leishmaniasis is caused by protozoan *Leishmania* parasites and is strongly associated with victims' living conditions, e.g. poverty, malnutrition, famine, illiteracy, and migrations. (Kumar, 2013). The disease has three major forms with different clinical manifestations (Handman, 2001), with Cutaneous Leishmaniasis (CL) being the most common type. CL can be transmitted by the bite of a female *Phlebotomus* sand fly (Swaminath et al., 2006), and considered to be a zoonosis which mostly has a gerbil specie as reservoir host (WHO, 1990). The disease is characterized by skin lesions, which typically develop within several weeks or months after exposure and results in severe scaring. No vaccine or drugs are available neither to prevent the infection nor to erase the scars. Even though the disease is treatable and preventable via reducing contacts with sand flies by using preventive measures, it remains a health hazard in many developing countries where such prevention is not possible. WHO reports have indicated that 1.5–2.0 million new cases of CL occurs each year worldwide (WHO, 2010). Among these cases, nearly 90% of CL cases currently occur in Iran, Syria, Saudi Arabia, Afghanistan, Algeria, Peru, and Brazil (Desjeux, 2004; Kumar, 2013, Gramiccia and Gradoni, 2005).

CL is the most frequent vector-borne disease in Iran, with an average of more than 22,000 cases in the last decade (Oshaghi et al., 2010). Isfahan province, at the center of Iran, has long been known as one of the most important endemic areas of CL (Arjmand et al., 2014; Nadim and Faghih, 1968) and still experiences a large number of annual infections, with approximately 2200 occurrence in 2013. CL resulting from *Leishmania major* and *Leishmania tropica* protozoa currently has epidemic status in Isfahan. *Rhombomys opimus*, a domestic rodent, is the main reservoir host and *Phlebotomus papatasi* is the most common CL sand fly vector in Isfahan (Emami et al., 2009). Despite numerous preventive measures of healthcare authorities and frequent research efforts during the last 30 years, the number of infections in Isfahan has remained prominent and the disease recently began spreading to the non-endemic regions of the province (Emami et al., 2009; Arjmand et al., 2014).

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The spatial distribution of CL as a vector-borne disease is

associated with the geographic range of its vectors and their habitat preferences (Kitron, 1998). Sampling of sand flies and determining the presence and abundance of intermediate host species is costly and time consuming (Kassem et al., 2012). The dispersion of sandflies and consequently the geographical distribution of CL can be influenced by environmental factors (Ferreira et al., 2001; Rispail et al., 2002; Kassem et al., 2012) and environmental and man-made changes such as fast-growing urbanization, development of new projects e.g., road building, mining, farming, forestry development, military activities and deterioration in social and economic conditions in the poor suburbs of cities (Desjeux, 2004; Dujardin, 2006; Adegboye and Kotze, 2012). Hence, the modeling of CL spread should comprise various environmental factors and also the interactions between the environment, sand flies and humans. Agent based models (ABMs), have the flexibility and capacity to incorporate these components. By simulating the individual behaviors, ABMs operate at a scale at which disease dynamics are based. Spatial analysis techniques can be applied with these simulation models to identify environmental patterns associated with CL vectors and are very helpful for identifying control strategies in unsampled areas (see Section 2). Hence, a spatial epidemiological approach was conducted in this study to analyze and evaluate the spread of CL by using an agent-based modeling method. The agent based method was chosen in this research because properly complied with requirements of such disease modeling problem (see Section 2 for details). The study area is mainly focused on Isfahan province in the central part of Iran (Fig. 1).

The rest of this paper is organized as follows. In Section 2, previous studies in modeling CL spread and the applicability of

agent-based models in disease modeling are explored. In Section 3, the local survey and data collection processes are described briefly. In Section 4, the model used for modeling CL dynamics is presented. The results are expressed in Section 5. Discussions and ideas for further work are represented in Section 6, and a short summary of the paper and the conclusions are presented in Section 7.

#### 2. Background

The impact of spatial analysis approaches on existing knowledge regarding CL spread and incidence cannot be ruled out. Previously, Nadim and Faghih (1968) considered geography in the epidemiology of CL. Lysenko (1971) presented one of the first attempts at CL mapping, in which the geographical distribution of CL cases was illustrated using cartographic maps. It took a while for researchers to consider spatial analysis as an explorative tool for CL epidemiology rather than as a visualization tool. Mott et al. (1995) introduced the application of geographical analysis for epidemiology and predictive modeling of Leishmaniasis. Thereafter, spatial analysis was used to identify and evaluate the underlying environmental precondition factors that influence the CL epidemic (Seid et al., 2014; Garni et al., 2014; Ali-Akbarpour et al., 2012). Resurfacing of Geographic information systems (GIS) highlighted the significant role of space when exploring the spread of CL. GIS has frequently been combined with statistical and cluster analysis methods to identify new CL epidemiological patterns (Salah et al., 2007; Rodríguez et al., 2013; Mollalo et al., 2015; Adegboye and Kotze, 2012). Spatial analysis methods have been utilized to generate CL risk maps (Seid et al., 2014; Garni et al., 2014; Ali-

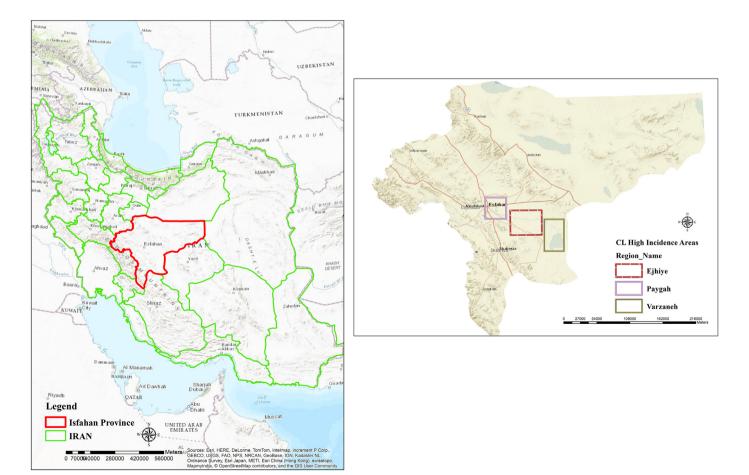


Fig. 1. Study area, Isfahan province, Iran.

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