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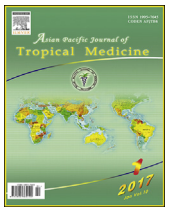

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Situation analysis of cutaneous leishmaniasis in an endemic area, south of Iran

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ABSTRACT

Objective: To update current situation of the cutaneous leishmaniasis (CL) in Kazerun County, southwest of Iran and to analyse the epidemiological aspects of the disease during 2005–2015.

Methods: Data on CL were obtained from the Health Center of Kazerun County, and then were analysed and mapped using SPSS and Arc GIS 10.3.

Results: A total of 700 cases of CL were recorded during the study period with an overall decreasing trend from 2005 to 2015. More than 60% of the patients were inhabitants of rural areas and males were infected more than females. Although there was not a significant difference between gender, job categories, residence and CL infection ($P > 0.05$), age groups were significantly different ($P < 0.05$). But there was no significant correlation between monthly cases of the disease with average temperature ($P > 0.05$). Most of the acute lesions were found to be present on the hand, leg and face, respectively. The average CL incidence in the study area was calculated as 24.9/100 000 population. A hot spot for the disease was found in southern part of the area ($P < 0.05$).

Conclusions: This study revealed that CL is present in Kazerun country. Thus, effective monitoring and sustained surveillance system is crucial in counteracting the disease, and if possible, to eliminate it.

1. Introduction

Leishmaniasis is an arthropod-borne disease caused by over 20 protozoan species belonging to the genus *Leishmania*. The Eastern Mediterranean region (EMR) of the World Health Organization (WHO) faces a major public health problem with regards to Leishmaniasis [1]. Four forms of the disease occur; Zoonotic Cutaneous Leishmaniasis (ZCL), Anthroponotic Cutaneous Leishmaniasis (ACL), Zoonotic Visceral Leishmaniasis (ZVL) and Anthroponotic Visceral Leishmaniasis (AVL). Three forms of the diseases (ZCL, ACL and ZVL) either independently or concurrently exist in 14 of the 22 countries of EMR region [2]. These countries include Afghanistan, Egypt, Iran, Iraq, Jordan, Libyan Arab Jamahiriya, Morocco, Pakistan, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia and Yemen. Many of the above-mentioned countries have experiences in the potential occurrence of the disease nearly an interval of ten years. Reports from WHO in 2008 confirmed that over 100 000 new cases have occurred in 12 countries in the EMR [2,3].

Epidemiologically, CL is presently endemic in 98 countries worldwide, including Iran [4]. It is estimated that between 500 000 and 1 000 000 new cases are reported annually in the world, however, due to under-reporting, only a smaller percentage (19%–37%) is verily reported to health systems. Among the reasons pertaining to CL under-reporting, the following three reasons are highlighted to play a key role. First, the refusal of patients to receive medical attention when the disease, presumed to cure by itself. Second, socioeconomic restraints hamper patients from medical care. Third, leishmaniasis is not incorporated in national policies as a serious public health problem [2].

Both urban and rural settings can experience outbreak of CL. Potentially severe, disfiguring and debilitating, CL infections exhibit lesions on infected individuals, especially on exposed

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parts of the body including the face, neck, arms and legs. Poverty has been partly linked to CL, as sufficient financial breakthrough is needed for treatment and case management [5].

In EMR countries, the causative agent of ZCL is the *Leishmania major* (*L. major*), and this is mainly transmitted by the bite of a female sand fly *Phlebotomus papatasi* (*P. papatasi*) [6]. Several factors contribute to the transmission of this disease, and these include, but not limited to, population movements (migration and the introduction of non-immunized individuals into areas of previous transmission), socioeconomic factors (poverty, poor housing and reduced sanitation) and environmental risk factors (high density of rodents, deforestation in some cases, and rodents) [7]. The cutaneous form of the disease (CL) also occurs in Iran, and closely associated with human environments. In the zoonotic forms of Leishmaniasis, vertebrate animals, with the exception of man, serve as reservoir hosts in which man is portrayed as the final host [5,8].

Contrary to the distribution of *L. major*, which necessarily depends on the presence of appropriate reservoir host, *P. papatasi* is widely distributed in semi-arid regions and feeds on both mammals and birds. In north-eastern and central areas of Iran, the great gerbil, *Rhombomys opimus* exhibits a host interaction with *L. major*, mostly active in semi-arid condition, and breeds mainly in spring, exposing them sand fly infection much earlier. Leishmaniasis is transmitted almost always by the bite of an infected sand fly, however other reports have revealed that the disease can also be transmitted through skin contact especially in CL [9].

The annual incidence of CL in Iran is averaged at 32 in 100 000 populations. It was reported in 2012 that the highest incidence was dominant in age groups of 1–4 and 5–9 years, projecting a respective incidence of 43 and 40 per 100 000 populations. Remarkably, males were more infected (57%) than females (43%) [10].

In addressing the issue of CL, the framework for action on CL in the Eastern Mediterranean region 2014–2018 has targeted surveillance techniques in detecting and reporting at least 75% of all CL cases within at-risk populations, case management skills in providing all detected CL cases accessible diagnostic and treatment intervention, reduction in the epidemiological exposure of CL in at-risk population and conducting sufficient and efficient research in curtailing the disease [11,12]. Epidemiologically, spatial distribution analysis of leishmaniasis has been recognized to be very essential in understanding the transmission of the disease, particularly in situations where a stronger correlation exist between spatial distribution of leishmaniasis and its hosts. Importantly, effective monitoring and evaluation is necessary in public health intervention for CL, and in the assessment of the betterment of service delivery to patient. This requires a considerate data collection and data analysis in ascertaining the efficiency of health interventions for CL. It is very well recommended by WHO to integrate surveillance system and control measures for leishmaniasis. A clear demarcation should be made between protection of individual hosts of the disease, and impeding leishmaniasis transmission by the use of community interventions [13].

Several studies have been conducted in Iran and based on their findings 17 out of 31 provinces of the country have endemic foci of CL [6]. It is confirmed climatic conditions influence the incidence of ZCL in Iran. The results of a study in this regard indicated that ZCL incidences in Golestan Province tend to be more prevalent in areas with higher temperature, lower relative humidity, lower total rainfall, higher evaporation and lower number of rainy days [14]. Another contributing factor in ZCL prevalence is age dependency. A study conducted in Qom province portrayed the most highly infected age group was 5–9 years old for ulcers with a rate of 6.56% [15]. Another study has recognized seasonal variations in ZCL incidence where the active season of *P. papatasi* extended from late April to early October in indoor areas [16]. This species is dominant in plain areas and lowlands [17–19]. A study conducted in Yazd Province, Central Iran, confirmed the rate of ulcers and scars among the inhabitants to be 24.6% and 30.4%, respectively. In that survey, endemic foci of CL has been detected in Yazd Province and the most highly infected age group was 10–14 with a rate of 28.4% [20]. An epidemiological study in Ardestan town in central Iran has indicated the most highly infected age group was 10–14 with a rate of 2.74% [21].

A modelling of CL distribution in Iran showed that over 60% probability of presence was considered as areas with high potential of CL transmission. These areas include arid and semiarid climates, mainly located in central part of the country [22].

Fars Province has the highest incidence of CL after Ilam in Iran and there are different foci of both ZCL and ACL in this province [10]. A nested-PCR epidemiological survey conducted in rural regions of Marvdasht, has confirmed the isolation of *L. major* as the agent and *P. papatasi* as the vector for leishmaniasis [23] Another study in Karameh district is in agreement with the fact *P. papatasi* is a vector responsible for the transmission of leishmaniasis [24]. Findings from a study in this province have demonstrated inter-and intragenic variations among *Leishmania* species and isolates from patients [25]. *Meriones libycus* has been shown to be the primary reservoir of ZCL in the rural areas of Arsanjan County in Fars province [26]. The close association of *Meriones libycus* and *P. papatasi* with human habitations in this province provides a convenient environment for CL transmission within the province. A post-earthquake epidemic of CL in rural Zarrindasht town has been studied, and the incidence of CL after the earthquake was significantly higher than previously recorded [27]. The above-mentioned studies show CL has different foci in Fars Province and therefore epidemiological studies are necessary to understand the pattern of the disease and its changes in the area to combat it appropriately.

The aim of this study was to update current situation of the CL in Kazerun County, south of Iran and to analyse the epidemiological aspects of the disease.

2. Materials and methods

2.1. Study area

This study was conducted in Kazerun, in the Fars Province of south-western Iran. The population of Kazerun as at 2011 was 254 704, including 67 290 families; out of them 53% are inhabitants of urban areas. It is situated on a plain among high limestone ridges on the north–south trunk road. The town is extensive, with well-built houses. The weather of the study area comprises of an average temperature of 31 °C, wind speed of 8 km/h and a humidity of 22%. The map of the study area is depicted in Figure 1.

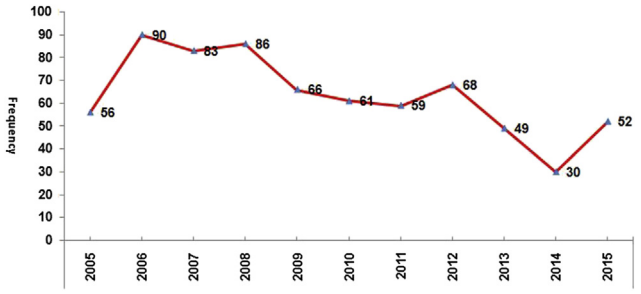

Figure 1. Frequency and trend line of cutaneous leishmaniasis cases in Kazerun County, south of Iran, 2005–2015.

2.2. Data collection and analysis

This descriptive analytical study was conducted during 2005–2015. Data on CL were extracted from the recording form for leishmaniasis patients obtained from the Health Center of Kazerun County. These forms have data such as gender, age, job, residential area, date of diagnosis, number of acute lesions on and their location on the body, history of travel and so on.

The *Chi* square test (X^2) was used to compare quantitative variables. The statistical analysis was conducted with statistical software SPSS (ver. 20). *P* values of 0.05 or less were considered statistically significant. Poisson regression was used to find correlation between mean monthly temperature and CL infection in the study area.

2.3. Spatial analysis of CL cases

Data on CL cases were located based on their inhabited places at the village level as well as urban areas. Shape files of the distribution of CL positive cases were prepared and classified using Arc GIS 10.3. Optimized Hot Spot Analysis (Spatial Statistics) was used to find hot and cold spots using the Getis-Ord Gi* statistic ($P < 0.05$).

3. Results

A total of 700 cases of CL were recorded during the study period with an overall decreasing trend from 2005 to 2015 (Figure 1). More than 60% of the patients were inhabitants of rural areas and there was not a significant different between residence in urban/rural areas and infection ($P > 0.05$) (Table 1). Males were infected more than females. There was not a significant difference between gender of patients in different years ($P > 0.05$). The most infected age group belonged to the 21–30 years with a significant difference between age groups in different years of the study period ($P < 0.05$). Considering the job, the most infected groups were house keepers and workers consisted more than 50% of cases. There was not a significant difference between job categories and CL infection ($P > 0.05$).

Temporal distribution of the disease showed 53% of cases recorded in autumn, followed by spring and winter, respectively (Figure 2). Monthly reports of the disease showed a peak in November (Figure 3). There was no significant correlation between monthly cases of the disease with average temperature in the same month, as well as one and two months earlier ($P > 0.05$).

Table 1
Frequency of CL according to some characteristics in Kazerun County, south of Iran during years of 2005–2015 [*n* (%)].

Characteristics	Values	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Total	Chi-square values	*P*-value
Residence	Urban	22 (39.3)	32 (35.6)	30 (36.1)	38 (44.2)	21 (31.8)	26 (42.6)	23 (39.0)	26 (38.2)	19 (38.8)	13 (43.3)	19 (36.5)	269 (38.4)	3.786	0.956
	Rural	34 (60.7)	58 (64.4)	53 (63.9)	48 (55.8)	45 (68.2)	35 (57.4)	36 (61.0)	42 (61.8)	30 (61.2)	17 (56.7)	33 (63.5)	431 (61.6)		
Gender	Male	36 (64.3)	52 (58.8)	45 (54.2)	53 (61.6)	36 (54.5)	32 (52.5)	37 (62.7)	26 (38.2)	26 (53.1)	21 (70.0)	30 (57.7)	394 (56.3)	15.661	0.110
	Female	20 (35.7)	38 (42.2)	38 (45.8)	33 (38.4)	30 (45.5)	29 (47.5)	22 (37.3)	42 (61.8)	23 (46.9)	9 (30.0)	22 (42.3)	306 (43.7)		
Age (year)	0–10	10 (17.9)	20 (22.2)	20 (24.1)	24 (27.9)	11 (16.7)	13 (21.3)	24 (40.7)	10 (14.7)	13 (26.5)	1 (3.3)	11 (21.2)	157 (22.4)	74.262	0.001
	11–20	18 (32.1)	22 (24.4)	17 (20.5)	18 (20.9)	14 (21.2)	10 (16.4)	7 (11.9)	14 (20.6)	3 (6.1)	10 (33.3)	8 (15.4)	141 (20.1)		
	21–30	11 (19.6)	23 (25.6)	30 (36.1)	28 (32.6)	23 (34.8)	18 (29.5)	11 (18.6)	16 (23.5)	14 (28.6)	10 (33.3)	21 (40.4)	205 (29.3)		
	31–40	8 (14.3)	11 (12.2)	11 (13.3)	10 (11.6)	11 (16.7)	8 (13.1)	8 (13.6)	14 (20.6)	6 (12.2)	9 (30.0)	5 (9.6)	101 (14.4)		
	>40	9 (16.1)	14 (15.6)	5 (6.0)	6 (7.0)	7 (10.6)	12 (19.7)	8 (15.3)	14 (20.6)	13 (26.5)	0 (0.0)	7 (13.5)	96 (13.7)		
Job	Rancher	5 (8.9)	3 (3.3)	5 (6.0)	4 (4.7)	3 (4.5)	2 (3.3)	4 (6.8)	3 (4.4)	3 (6.1)	1 (3.3)	3 (5.8)	36 (5.1)	69.673	0.184
	Worker	21 (37.5)	17 (18.9)	20 (24.1)	19 (22.1)	20 (30.3)	19 (31.1)	13 (22.0)	20 (29.4)	12 (24.5)	10 (33.3)	14 (26.9)	185 (26.4)		
	Housekeeper	14 (25.0)	29 (32.2)	29 (34.9)	24 (27.9)	21 (31.8)	18 (29.5)	8 (13.6)	25 (36.8)	12 (24.5)	9 (30.0)	15 (28.8)	204 (29.1)		
	Driver	3 (5.4)	5 (5.6)	3 (3.6)	2 (2.3)	1 (1.5)	2 (3.3)	5 (8.5)	1 (1.5)	2 (4.1)	1 (3.3)	4 (7.7)	29 (4.1)		
	Military	1 (1.8)	4 (4.4)	2 (2.45)	1 (1.2)	0 (0.0)	1 (1.6)	1 (1.7)	0 (0.0)	1 (2.0)	2 (6.7)	3 (5.8)	16 (2.3)		
	Student	7 (12.5)	14 (15.6)	7 (8.4)	14 (16.3)	10 (15.2)	9 (14.8)	5 (8.5)	13 (19.1)	5 (10.2)	4 (13.3)	6 (11.5)	94 (13.4)		
	Under school age	5 (8.9)	18 (20.0)	17 (20.5)	22 (25.6)	11 (16.7)	10 (16.4)	23 (39.0)	6 (8.8)	14 (28.6)	3 (10.0)	7 (13.5)	136 (19.4)		

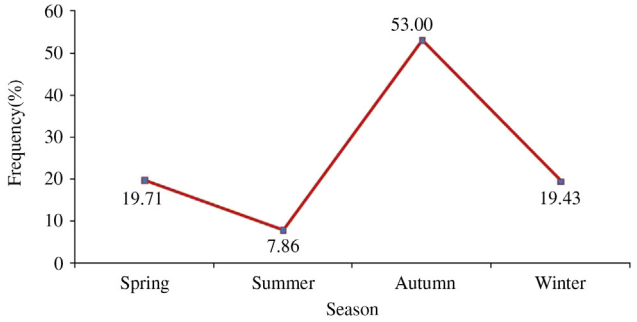

Figure 2. Distribution of CL according to the seasons in Kazerun County, south of Iran, 2005–2015.

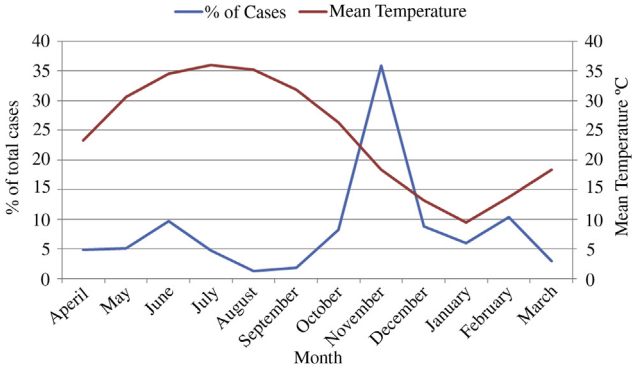

Figure 3. Monthly reports of CL and mean monthly temperature in Kazerun County, south of Iran, 2005–2015.

Most of the acute lesions were found to be on hand (44.00%), leg (27.57%) and face (23.29%), respectively, 3.14% lesions were on other parts of the body. The average of CL incidence in the study area was calculated as 24.9/100 000 population. A survey on the history of travel among the patients showed 46.6% had at least one travel to other areas of the province or the country (Figure 4).

Spatial distribution of the diseases in urban and rural areas showed a total of 53 villages/localities had the CL cases, although 13% of the cases were living in Kazerun city. The cumulative distribution map of the disease across the county showed it was more prevalent in north-east and southern parts of the study area (Figure 5). Optimized hot spot analysis showed non-significant correlation for CL cases in most villages/localities of the study area, however one hot spot was found in southern part ($P < 0.05$).

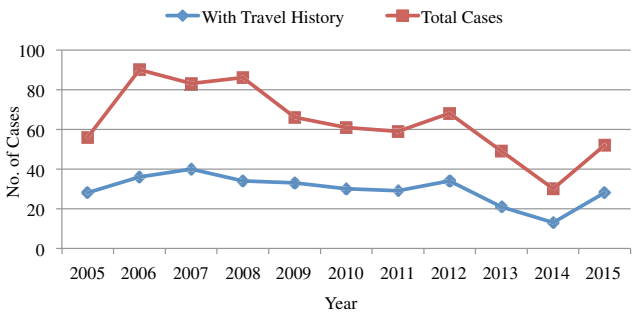

Figure 4. Cases of CL based on travel history in different years, Kazerun County, south of Iran, 2005–2015.

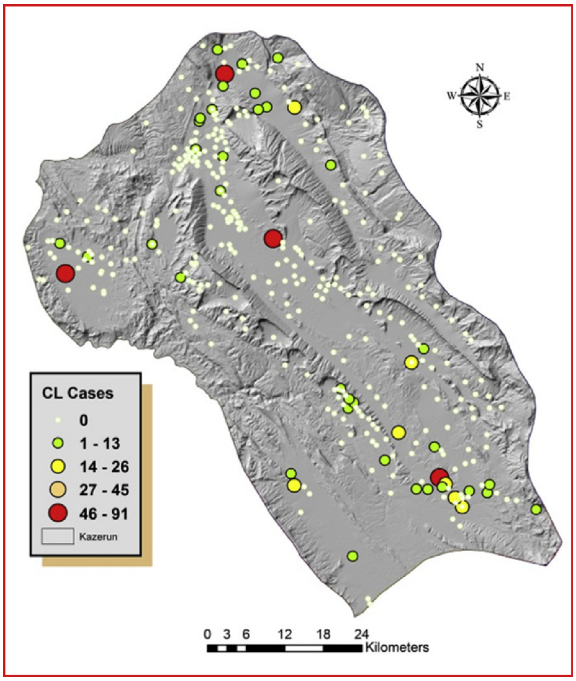

Figure 5. Cumulative distribution map of CL cases across Kazerun County, south of Iran, 2005–2015.

4. Discussion

Leishmaniasis, caused by *L. major*, has been discovered to be endemic in many EMR countries including Iran [6]. In the present study, there was a decreasing trend of CL during the study period. Rural areas recorded the largest cases of CL (60%), and the incidence of the disease differed among cases recorded in the rural and urban areas ($P > 0.05$). A previous study conducted in Marvdasht, Fars Province showed that rural areas had the highest number of cases, and these cases were mainly due to *L. major* infections [26]. Fars Province has the highest incidence of CL after Ilam in Iran [10]. In rural areas, people are more prone to the bite of sand flies, and are in close proximity to gerbils which serve as reservoirs for *L. major*. A post-earthquake epidemic of CL in rural Zarrindasht town of Fars province has been studied, and the incidence of CL after the earthquake was significantly higher than previously recorded [27]. These findings show Fars province is a vulnerable area for CL transmission. Previous studies on probability of presence of both vectors and reservoir hosts of CL showed Fars province is an area with high vulnerability for the disease transmission [8,23].

Males were more infected than the females ($P > 0.05$). Males are more associated with farming activities in rural areas, and therefore are in close contact to wandering sand flies. Earlier, numerous studies in Iran, and particularly Fars province, have demonstrated males are highly infected and readily susceptible to CL [10].

Age-dependency nature of the disease was also recognized in this study. After analysis of the results of this study, the most infected age group belonged to 21–30 years during the study period ($P < 0.05$). This age group normally encompasses the youth, which are mostly active throughout the day, engage in most outdoor activities, particularly in working areas. An epidemiological study in Ardestan town in central Iran has

indicated the most highly infected age group was 10–14 with a rate of 2.74% [21]. Although our results is quite different from the results of the study conducted in Ardestan town, it is worthy to note that a majority of CL patients resided in rural areas of Kazerun, which might have contributed to an older age group of 21–30 years.

CL cases differed significantly among patients of different job categories, and the most infected individuals were mainly house keepers and workers who entails more than 50% of the overall cases recorded ($P > 0.05$). The workers are mostly found in outdoor places where sand flies are more prominent, and therefore are at higher risk of getting the disease. These workers normally spend most of their time during the day in areas where sand flies are more common. House keepers are mostly wives of the workers and sometimes assist their couples in working environments during their leisure time, and as a result contract the disease through the bite of phlebotomine sand flies.

Seasonal variation effects were observed in this study. Autumn recorded the highest temporal distribution of CL (53%). A previous study conducted by Yaghoobi-Ershadi and Javadian [17] illustrated temporal distribution of sand flies in different Provinces, and realized that the activity of sand flies almost stopped in cold season, while during May–September there is at least one record of phlebotominae sand flies from almost all provinces. Considering the peak of activity of sand flies in September in the inland areas [6] and a latency period of 2–8 weeks for zoonotic cutaneous leishmaniasis (ZCL) it seems this form of the disease circulates in Kazerun County as well, although parasitological studies are recommended for detection of the parasite species in local cases of CL. In this study, a peak of CL cases was evident in November. This is in accordance with other foci of the diseases in Iran. Although in our study average temperature did not play a major role in monthly reported CL cases, another study in northeast of the country [14] found higher prevalence of CL in the area with higher temperatures.

The part of the body of the patients mostly bitten was the hand, leg and face in that order. Obviously, these parts of the body are mostly exposed and therefore provide a larger surface area for sand fly bites. This results is in accordance with a previous study performed in Ghanavat Rural District, Qom Province, Central Iran, where the highest number of ulcers as a result of numerous sand fly bites occurred on the hands (51.6%) [15].

After analysis of the data, the average incidence of CL in the study period was delineated as 24.9/100 000. The incidence of CL in the country has been previously calculated to be 32/100 000 [10]. Although this difference is not considerable, perhaps, the decline of the incidence of the disease in this study may be due to proper surveillance system and effective intervention over the years or lower vulnerability for transmission. More efforts are needed to curtail the disease, and if possible, to eliminate it completely.

Travel to or from endemic areas may contribute to wider distribution of the disease, and heighten the disease burden in the province and the country at large. In the present study, nearly 46% had at least a history of travel to endemic areas. Although ZCL is transmitted from gerbils to human by the bite of infected sand flies, anthroponotic form of CL is also common in some parts of the province and the country as well and *Phlebotomus sergenti* as its vector is reported from different areas of Fars province [17]. This form of the disease can be transmitted from human to human, so imported cases should be considered as a probable hazard.

In view of the spatial distribution of CL, 53 villages' harboured the disease, while 13% of cases were living in Kazerun city. Here, villages were more prone to leishmaniasis, because residents of these areas normally engage in agricultural activities, and are readily exposed to the bite of infected sand flies which are mainly living and breeding in the gerbil burrows, and the consequent leishmaniasis infection. Our findings were contrary to a previous study in Hamadan province. It may be due to local transmission of the disease in Kazerun, while CL cases seem to be imported in Hamadan [28]. In this study, a hot spot of the disease was found in southern parts of the study area ($P < 0.05$), an indication for local transmission in this area.

More studies are recommended to find the details of CL transmission cycle including vector, reservoir and parasite in these two clusters, to combat the diseases successfully.

Conflict of interest statement

We declare that we have no conflict of interest.

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