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Geospatial Health 2017; volume 12:478

Impact of climate variability on the occurrence of cutaneous leishmaniasis in Khuzestan Province, southwestern Iran

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Abstract

Leishmaniasis, one of the most important parasitic diseases worldwide, is frequently cited with respect to health risks related to climate change. The current variability of the climate may have different impacts on the transmission of cutaneous leishmaniasis (CL) depending on the various Leishmania species. The number and distribution of CL cases in Khuzestan Province, Southwestern Iran was analysed over the 2010-2014 period with regard to temperature, humidity, rainfall, sunshine hours, evaporation and wind-related climate issues. During the study period, there were 4672 recorded clinical cases of CL, the incidence of which was found to fall into three types of areas, such as high, intermediate and low-level endemic areas. Compared to the intermediate and low-endemic areas, the hyper-endemic areas showed significantly variable meteorological data with regard to rainy days, maximum/minimum temperature and humidity. Decreased temperatures in the eastern part of this province were found to promote the disease towards its centre. We conclude that the meteorological variables and incidence data of CL indicate that the number of rainy days, maximum and minimum temperatures and relative humidity are significant variables that can predict CL incidence. Indeed, the substantial climatic variability occurring during the recent 5-year period (2010-2014) in Khuzestan Province could be the main reason for the change in epidemiology and transmission of CL.

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Key words: Cutaneous leishmaniasis; Climate variability; Epidemiology; Khuzestan; Iran.

Acknowledgments: the authors would like to appreciate Shahrekord University, Control Disease Center of Khouzestan Province and Shiraz Molecular Pathology Lab Research Center. We also would like to thank Ms Shojaeefard.

Contributions: SS designed the study; FA and SS contributed to writing of the manuscript; TA and SJ collected and analysed the data. All the authors read and approved the manuscript.

Received for publication: 7 April 2016.
Revision received: 18 October 2016.
Accepted for publication: 18 October 2016.

Geospatial Health 2017; 12:478
doi:10.4081/gh.2017.478

Introduction

Leishmaniasis is among the six most important, parasitic diseases of the world affecting 88 countries in almost every continent (Desjeux, 2004). It is estimated that more than 350 million people are at risk for this disease with 15 million already infected with an additional 1.5-2 million new infections annually (Shirian *et al*., 2013). Despite advances in diagnosis and treatment, leishmaniasis is now considered a severe public health problem, particularly in developing countries, such as Iran, exerting a great economic burden on available health resources (Asgari *et al*., 2007). The disease is complex with different clinical presentations such as visceral, cutaneous and muco-cutaneous forms (Shirian *et al*., 2012a, 2012b, 2014; Oryan *et al*., 2013). Cutaneous leishmaniasis (CL) is disabling and presents with a remarkable variability of the clinical manifestations such as multiple lesions, which are frequently self-healing in the old world. It is the most common form of the disease in Iran (Shirian *et al*., 2016), where transmission occurs through the bite of the infected female *Phlebotomus* sand fly (Asgari *et al*., 2007; Shirian *et al*., 2012).

Khuzestan Province in Southwestern Iran is one of the important foci of the disease (Beiranvand *et al*., 2014). Among the various, ecological factors associated with the distribution of the vectors of the disease, *Phlebotomus* species in the Old World and *Lutzomyia* species in the New World, global climatic changes seem to be a critical factor. As the case with other vector-borne diseases, *e.g*. Lyme disease, malaria, fascioliasis, Rift Valley fever, and schistosomiasis, leishmaniasis appears focally focal in areas characterized by situations where the spatial distribution of parasite, host, vector and required environmental conditions coincide. Being based on the spatial component with a varied input of environmental variables, geographic information systems (GIS) lend themselves to the study of vector-borne diseases. In addition, data from different scales and types, including population health data, can be integrated with environmental data as well as climatic information. Leishmaniasis is naturally related to environmental change and climate (Correa Antonialli *et al*., 2007) and its transmission relies on a complex cycle where the environment has a significant influence (Fonseca Eda *et al*., 2014). Climate variability may have different impact in the transmission of CL depending on the various *Leishmania* species and their particular vectors in the different regions of the world (Rodriguez-Morales, 2005). Our study represents an attempt to evaluate the impact of climate variability on the number of human cases and their distribution in the Southwestern region of Iran where Khuzestan Province is located.

Materials and Methods

Study area and population

Khuzestan Province is located in the Southwestern Iran at 29°57′-33°0′N and 47°38′-50°32′E and covers approximately 63,238 km^2, which is 3.9% of the total surface area of the country (Figure 1). This province is subdivided into 24 districts and 126 counties characterized by an environment that is most often dusty and dry with warm summers, mild winters and a great deal of sunshine throughout the year. The climate of Khuzestan is generally very hot and occasionally humid, particularly in the South, while the winters are relatively cold and also dry. Summer temperatures routinely exceed 45°C (113°F) and can in the winter drop below the freezing point with occasional snowfall as far south as Ahvaz Dstrict. The maximum temperature occasionally soars to 55°C (131°F) and can at times reach close to 60°C. The most recent census shows the province having an estimated population of 4,277,998 inhabitants (Beiranvand *et al*., 2014). The study included all residents in Khozestan and we analyzed the impact of climatic variability on the incidence of CL cases during the 5-year period from January 2010 to December 2014, including temperature, humidity, rainfall, sunshine hours, evaporation, and wind speed.

Collected data

Climate data

Monthly eco-environmental and climate data including monthly total rainfall, monthly average minimum and maximum temperatures, average relative humidity, sunshine hours, average evaporation and wind speed for the period 2010-2014 were obtained

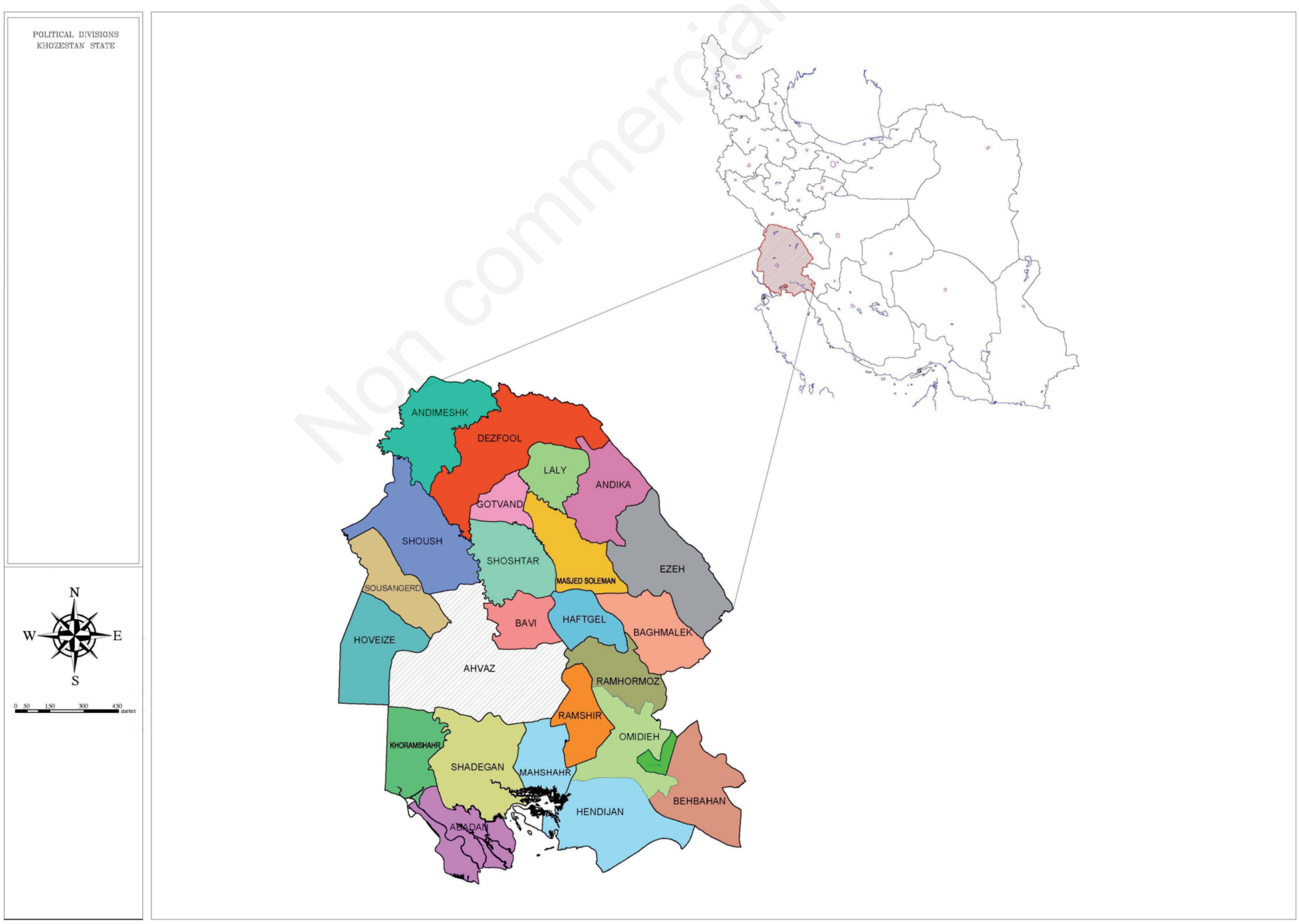

Figure 1. Map of Khuzestan Province, southwestern Iran with all districts.

from the weather bureau of Khuzestan Province that routinely collects information from meteorological stations in different formats as described by Srimath-Tirumula-Peddinti *et al*. (2015).

Cutaneous leishmaniasis incidence

Monthly CL incidence and epidemiological data at the district and village levels for the period 2010-2014 from the health surveillance systems in all counties were provided by the Centre of Disease Control (CDC) of Khuzestan Province.

Statistical analysis

ArcGIS 9.3 software (http://www.esri.com/software/ arcgis/) was used. The CL incidence was evaluated by GIS maps according to climatic and vegetation at the 1:25,000 scale (Ostad *et al*., 2016). The data were used to map the prevalence and incidence of CL disease and also to evaluate the statistical relationship of the climatic factors.

Mapping of cutaneous leishmaniasis disease

The CL disease incidence data were aggregated by CDC by city or district, by month, and by year. Aggregated CL incidence data for the five years (2010-2014) were used to map the CL disease incidence in each city or district. Maps representing disease incidence were developed based on calculation of the number of infected cases out of the total human population for the same period sorting data from the highest to the lowest disease incidence for each city/district as follows:

$$\text{Percentage of CL cases} = \frac{\text{Number of infected cases}}{\text{Total district population}}$$

Correlation between climatic variables and cutaneous leishmaniasis disease

Correlation coefficient analysis was used to observe the relationship between climatic factors, such as temperature, rainfall and relative humidity, windy days and hours of sunshine hours, and the total number of CL cases as well as the number of new cases. In this case, all the data points on climatic factors and disease incidence were aggregated on a monthly basis in the districts.

Modelling climatic factors and cutaneous leishmaniasis disease incidence

Linear regression analysis and auto regression analysis were used to model and predict the monthly CL disease incidence. In this case, district data on CL disease incidence, relative humidity, sunshine hours, windy days, temperature and rainfall were simply aggregated by month for each year. Comparisons of annual proportional changes and climatic variations according to the different seasons in terms of departure from the annual mean number of CL cases and in the mean number of cases per season for each area were performed. In addition, linear regression models to assess the temporal CL incidence variability on CL were used. Descriptive statistics (mean, frequency) and inferential statistics analyses were done using the SPSS 22.0 software package with 95% confidence interval.

Results

Epidemiological results

There were 4672 recorded cases of clinical CL in Khuzestan Province in the 5-year study period, during which substantial climatic variability was also identified. The majority of cases were seen in Ahvaz followed by Hoveizeh and Sousangerd, the three districts located in the Centre-east of Khuzestan, while sporadic events (under 1% of cases) were observed in Laly, Gotvand and Andika districts in the East (Figure 2). Hoveizeh showed the highest incidence of CL in 2010. However, most of recorded patients lived near the border to Hovizeh with Ahvaz and Suosangerd in this year. Based on CL incidence, Khuzestan Province could be divided into three regions including high (>100 cases), intermediate (50-100 cases) and low-level endemic or non-endemic areas (mean 0-50) (Table 1). This table also shows that there has been an overall diminishing trend during the 5-year period moving from 1363 patients (29.1%) in 2011 to 420 patients (8.98%) in 2014. However, a new CL focus did appear in 2011 in Hafkeil, a district located in the centre of Khuzestan Province (Table 1).

Table 1. The incidence rate of cutaneous leishmaniasis in different districts of Khuzestan Province, southwestern Iran (2010-2014).

Type of areas	District	Year 2010	2011	2012	2013	2014	Incidence rate (%)
High incidence areas	Hoveizeh	127	127	671	53	27	1.4
	Ramshir	98	98	73	73	74	1.2
	Sousangerd	192	192	75	84	75	0.6
Intermediate incidence areas	Ahvaz°	345	340	192	172	118	0.1
	Shoshe	89	90	64	52	0	0.2
	Behbahan	64	76	68	54	0	0.23
Areas of low incidence or none	Laly	4	7	6	4	5	>0.1
	Hendijan	8	9	16	10	0	>0.1
	Shadegan	11	7	15	11	0	>0.1
	Omideh	10	5	5	15	3	>0.1
	Dezfool	0	0	0	0	0	>0.1
	Haftghil#	0	4	6	5	0	>0.1
	Other cities	208	102	167	113	115	>0.1
Total		1066	1062	1363	661	420	-

°The highest number of cases in this period, but the incidence rate was less than 0.1%; #new focus in 2011.

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Seasonality of CL was mainly restricted to the October–February period with the main peaks occurring in December and January (Figure 3). Annually, the highest number of cases was generally observed in January (20.93%), December (14.98.1%), February (14.57%), November (9.73%) and October (7.87%). Major and minor outbreaks of CL occurred in 2011 and 2013, respectively.

Cutaneous leishmaniasis mapping

Out of Khuzestan's 24 districts, Hoveizeh, Ramshir and Sousangerd had the highest rate of infection with 1.4, 1.2 and 0.6%, respectively, while the remaining districts were below 0.2% of the infectivity rate (Figure 2). The obtained data revealed that the majority of the cases belonged to Ahvaz followed by Hoveizeh and Sousangerd in that order. However, Hoveizeh, Ramshir and Sousangerd had the highest rate of infection with 1.4, 1.2 and 0.6%, respectively, and the remaining districts were below 0.2% (Figure 2, Table 1). We also noted a considerable decrease in the number of cases in 2014 and a slight increase in 2012 (Figure 4).

Meteorological results

With regard to the meteorological data (Table 2), a trend similar to that described above for the CL cases was recorded in the mean climate parameters, such as rainfall, temperature and relative humidity in 2012 (Figure 4) that is shown here to underline the importance and magnitude of these parameters. Overall, the data (Table 2) show that Ahvaz, followed by Hoveizeh and Sousangerd, had the highest mean temperatures and humidity values in the summer. Among the hyper-endemic districts, however, Hoveizeh showed a higher number of rainy days and higher relative humidity than Ahvaz and Sousangerd in 2012. The mean maximum and minimum temperature, as well as humidity and the number of rainy days, in the high-incidence areas was significantly higher than that of the intermediate and low incidence areas (Figure 3). In addition, the peak temperatures and humidity values were recorded in 2012, while the weather bureau of Khuzestan Province recorded the lowest temperature in the eastern part of the province in 2011. The magnitude of the CL problem can be observed from the annual case records, which shows variations of the CL disease incidence for all the districts of Khuzestan Province (Figure 4).

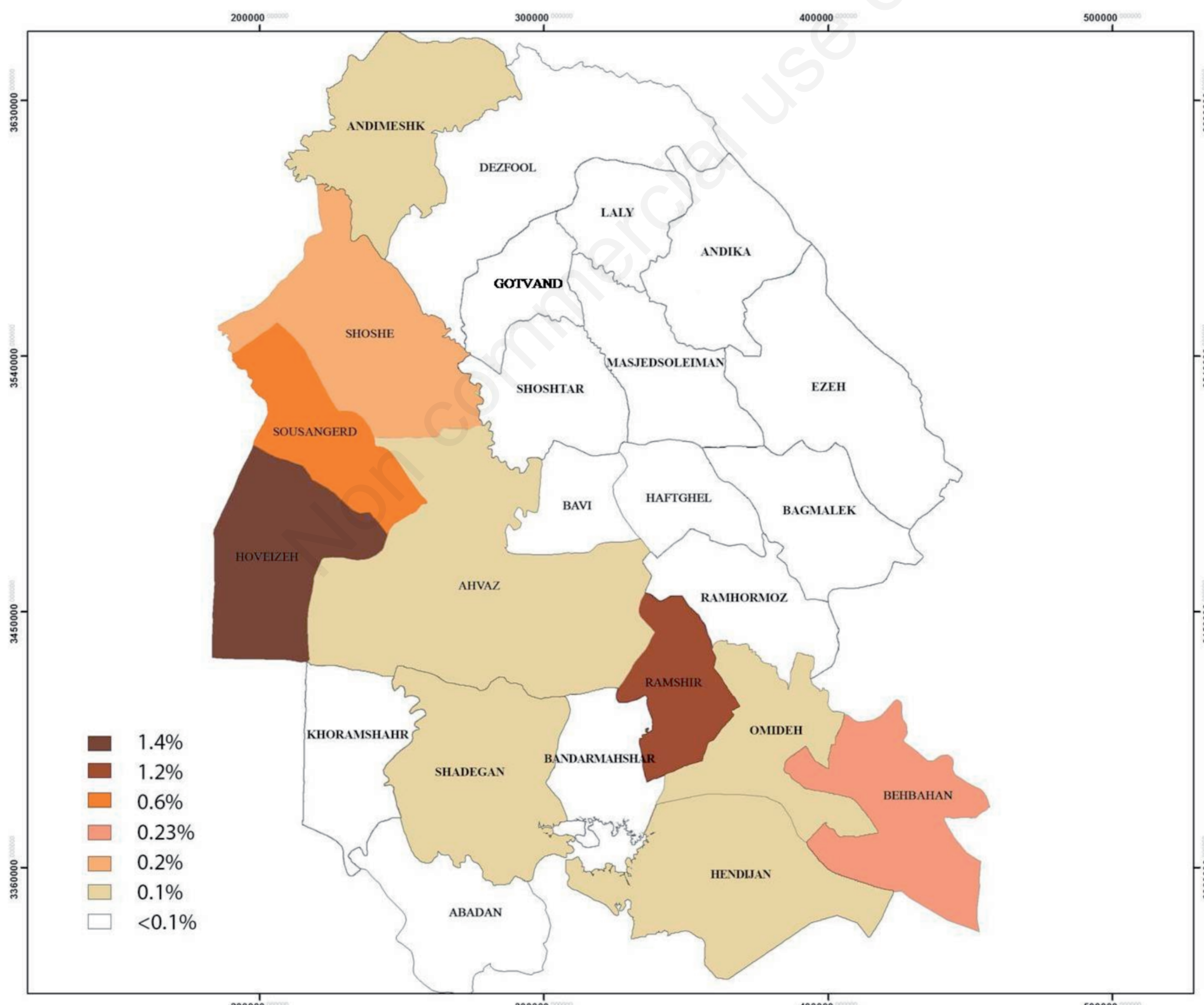

Figure 2. Incidence rate (%) of cutaneous leishmaniasis in the 24 districts of Khuzestan Province, southwestern Iran (2010-2014).

Correlation of climatic factors and cutaneous leishmaniasis incidence

A positive, significant association was observed between total rainfall and humidity on the one hand and CL incidence on the other (Figure 5, Table 3). Average maximum temperature, humidity and rainfall had a significant impact on the disease incidence (Figure 4). Although a negative, significant relationship was observed between the monthly temperature and evaporation on the one hand and the CL incidence on the other (Figure 5, Table 3), higher number of patients were seen in the years with the higher mean temperatures, especially in the activity months of sand fly activity.

Table 2. Classification of Khuzestan Province, southwestern Iran based on cutaneous leishmaniasis incidence and mean climate changes over five years (2010-2014).

Climate variables	High rate				Intermediate rate		Low rate or none			P
	Hovizeh	Ramshir	Sousangerd	Ahvaz	Behbahan	Shoshe	Dezfool	Haftghil	Omideh	
Rain (days)	65±11.4 (52-74)	62.6±7.2 (50-68)	61.2±7.9 (50-68)	58.2±5.4 (48-61)	55.0±4.1 (49-60)	55±4.5 (50-62)	42.4±8.2 (30-53)	42.6±6.8 (32-51)	42.8±6.9 (34-52)	0.04
$Temp_{max}$ (°C)	47.4±2 (44-49)	47.2±2 (44-48)	47.2±2 (44-48)	44.4±2 (40-45)	42.2±2 (40-44)	42.2±2 (40-44)	38.0±1.5 (36-40)	35.2±2.5 (32-38)	34.8±2.2 (33-37)	0.03
$Temp_{min}$ (°C)	4±1.5 (2-6)	3.8±1.9 (1-6)	3.8±1.3 (2-5)	1.2±1.6 (-1-3)	0.3±1.6 (-2-2)	0.3±1.6 (-2-2)	-1±1.5 (-3-0)	-1±1.5 (-3-0)	-1±1.5 (-3-0)	0.05
Wind speed (m/sec)	13.4±4.1	13.6±3.7	13.5±3.8	12.8±3.3	13.8±4.1	13.6±2.3	14.1±2.3	13.8±3.1	13.4±3.6	0.2
$Humid._{max}$ (%)	78±4 (74-84)	77.8±2.7 (75-82)	78.8±2.3 (76-80)	62.8±5.9 (52-68)	57.8±4.3 (52-66)	57.8±3 (54-62)	48.8±4.1 (44-54)	48.8±3.8 (44-53)	46.6±2.7 (43-50)	0.01
$Humid._{min}$ (%)	21.2±2.3 (18-24)	21.4±2.7 (18-26)	19.8±1.4 (18-22)	18.4±1.5 (17-20)	18.4±1.5 (17-20)	18.4±1.5 (17-20)	12.2±1.3 (10-14)	10.8±1.9 (8-13)	10.8±1.9 (8-13)	0.02
Evaporation (mm)	23±1.5 (21-25)	23±1.5 (21-25)	22.8 ±1.9 (20-25)	21.6±1.5 (19-22)	19.6±1.6 (18-22)	20.1±1.6 (18-23)	18.2±1.4 (16-20)	16.4±1.8 (14-18)	16.4±1.8 (14-18)	0.6
Sun (hours)	296±6.2 (288-303)	297±6.1 (289-303)	298±6.4 (288-304)	297 ±9.1 (286-310)	299 ±6.9 (290-309)	298 ±5.6 (292-307)	299 ±7.9 (290-313)	296±6.2 (288-303)	297 ±9.2 (287-310)	0.4

Values are expressed as mean±standard deviation (span).

Table. 3. Correlation of cutaneous leishmaniasis incidence and climate variables.

Rainfall	Evaporation	Humidity	Temperature	CL	Parameter
				r=1	CL
			r=1	r=-0.679*	Temperature
		r=1	r=-0.935**	r=0.632**	Humidity
	r=1	r=-0.944**	r=0.968**	r=-0.639**	Evaporation
r= 1	r=-0.704**	r=0.802**	r=-0.688**	r=0.402**	Rainfall

CL, cutaneous leishmaniasis. *Correlation at P=0.05; **correlation at P=0.01.

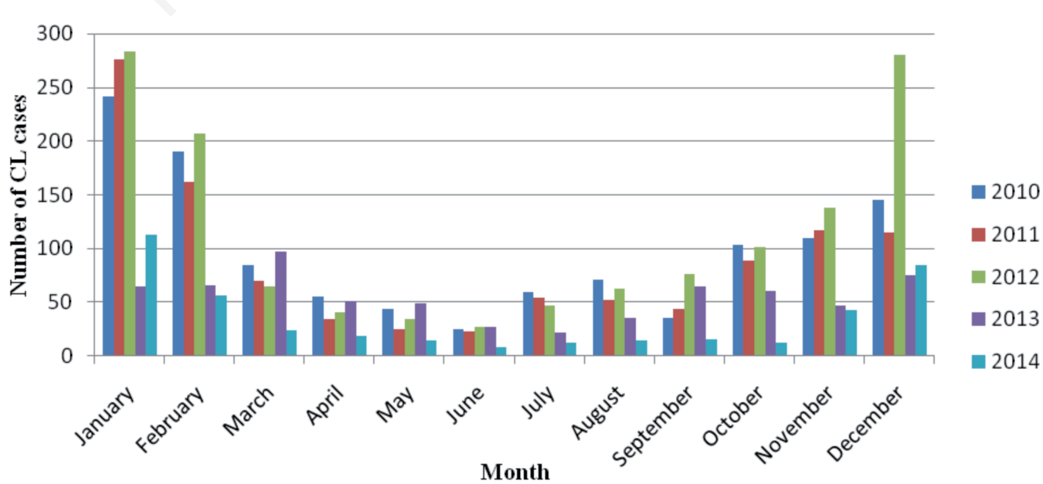

Figure 3. Incidence of cutaneous leishmaniasis in Khuzestan Province, southwestern Iran (2010-2014).

Discussion

Prediction of the impact of climate change on the epidemiology and number cases of infectious disease such as leishmaniasis is a pressing challenge. The primarily aim of this study was to investigate, for the first time, the impact of climate variability in the number and distribution cases in the Khuzestan Province in southwestern Iran. Among the various ecological factors associated with the distribution of *Phlebotomus* species in the Old World, climate seems to play a critical role with indications of potential changes in the geographical distribution of certain vectors, including sand flies (Sutherst, 2004; Rodriguez-Morales, 2005). As can be seen in Table 2, the meteorological variables and incidence data of CL indicate that the number of rainy days, maximum and minimum temperatures and humidity are significant variables that can predict CL incidence ($P<0.05$).

The importance of environmental variables, climate factors in particular, is supported by our finding of the CL incidence rates varied geographically in such a way that three typical areas with substantial differences appeared: highly endemic areas contrasting with low or non endemic areas, including some places with intermediate levels of disease. The collected data from CDC of Khuzestan Province show that majority of the intensive CL events in the five years of the study occurred in Ahvaz, followed by Hoveizeh, Sousangerd and Ramshir districts that also had the highest summer temperatures and rainfall or humidity. However, the latter three districts have lower populations than that of Ahvaz, which introduces an element of increased statistical uncertainty.

The positive correlation observed between increased, annual temperatures and the monthly rainfall/humidity on the one hand and CL incidence on the other, as well as its negative association with the monthly temperature, can be directly related to sand fly activity. However, this is not the only potential explanation for the recent variation in the distribution of leishmaniasis in Khuzestan. It should also be noted that incidence of this disease starts in the early autumn and reaches its peak in January and February in Khuzestan Province. The positive relationship between annual temperature with CL incidence and the negative correlation between monthly temperature and CL incidence can therefore also be attributed to the incubation period of the disease since the symptoms start to appear between two and six months after contact between sand fly and patient and never less than two months. Thus, as the peak of heat in Khuzestan Province (June, July, and August) is the most appropriate time for sand fly activity, the CL incidence in the autumn could well be due to sand fly bites 2-6 months ago. Seen in this light, the decrease in CL incidence during the spring could be explained by the unfavourable climatic conditions for sand fly activities during the winter.

Several factors have been suggested as contributed to altering epidemiological patterns and the re-emergence of vector-borne diseases such as climate variability (Shimabukuro *et al*., 2010). Temperature and relative humidity play an important role in survival of the sand fly vector, its development and activity (Dereure *et al*., 2009). Review of meteorological data reveal that rainy days and the mean humidity in this region (Hoveizeh) was higher than in Ahvaz and Sousangerd, while, the mean summer temperatures in Ahvaz and Sousangerd were found to be higher than that of Hoveizeh during this year. Since most patients on record live on the border of two other endemic areas in Hoveizeh, it is thought that reservoirs and vectors of the disease have migrated from the dry and hot regions of Ahvaz and Sousangerd to the humid and

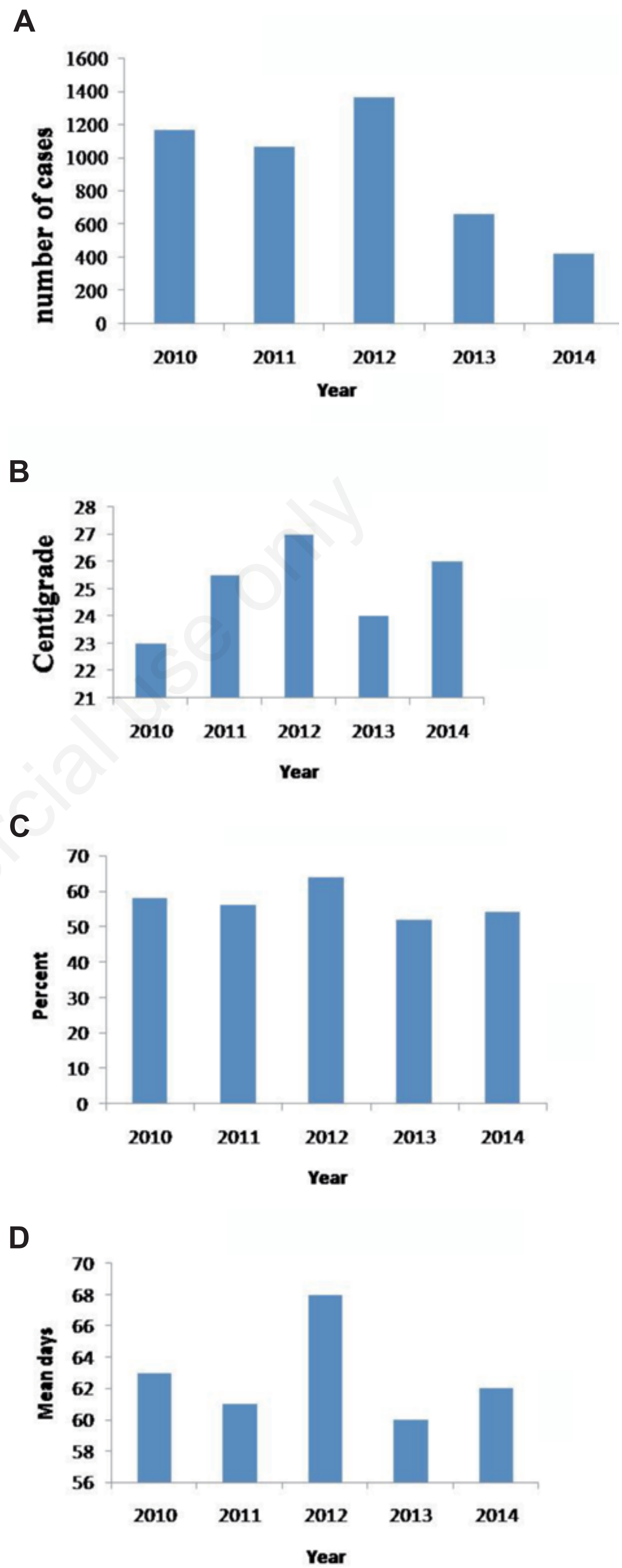

Figure 4. Data of cutaneous leishmaniasis cases presented by year (A), mean temperature (B), mean humidity (C), and mean rainy days (D) in all districts of Khuzestan Province, southwestern Iran.

warm areas of Hoveizeh. CL incidence and climate data indicate that the hyper-endemic areas for CL had significantly different climate variability with regard to the number of rainy days, maximum/minimum temperatures and humidity compared to intermediate and hypo-endemic or non-endemic areas.

It has been demonstrated that vector populations are affected by humidity, temperature, vegetation, land-cover and light availability (Shimabukuro *et al*., 2010). Indeed, recent evidence shows that changes in temperature and precipitation have already changed the distribution and behaviour of vectors and in consequence also the epidemiology of vector-borne diseases, for example by changing the length of the life cycle of the parasite (Tabachnick, 2010). With a higher mean temperature, the sand fly larvae will take a shorter time to mature, thereby increasing the capacity to produce more offspring during the transmission period (Rueda *et al*., 1990; Khasnis and Nettleman, 2005). Our results show that the major and minor outbreaks of CL that occurred in 2012 and 2014, respectively, and the meteorological data obtained concur that the peak temperature and humidity occurred in 2012. In this year (2011), Khuzestan's weather bureau recorded the lowest temperature in the East of this province. Since temperature plays an important role for the sand fly life cycle, it could be one of the main factors promoting the spread of CL from the eastern part of the province to the centre. The new CL focus seen in Hafkeil in 2011 is an indication of this change. The diminishing trend of CL cases in Khuzestan Province during the 5-year study reported here is a separate development having less to do with prevailing weather situation than sustained progress by the national CL control programmes working in these regions based on epidemiological situation and stratification of risk areas.

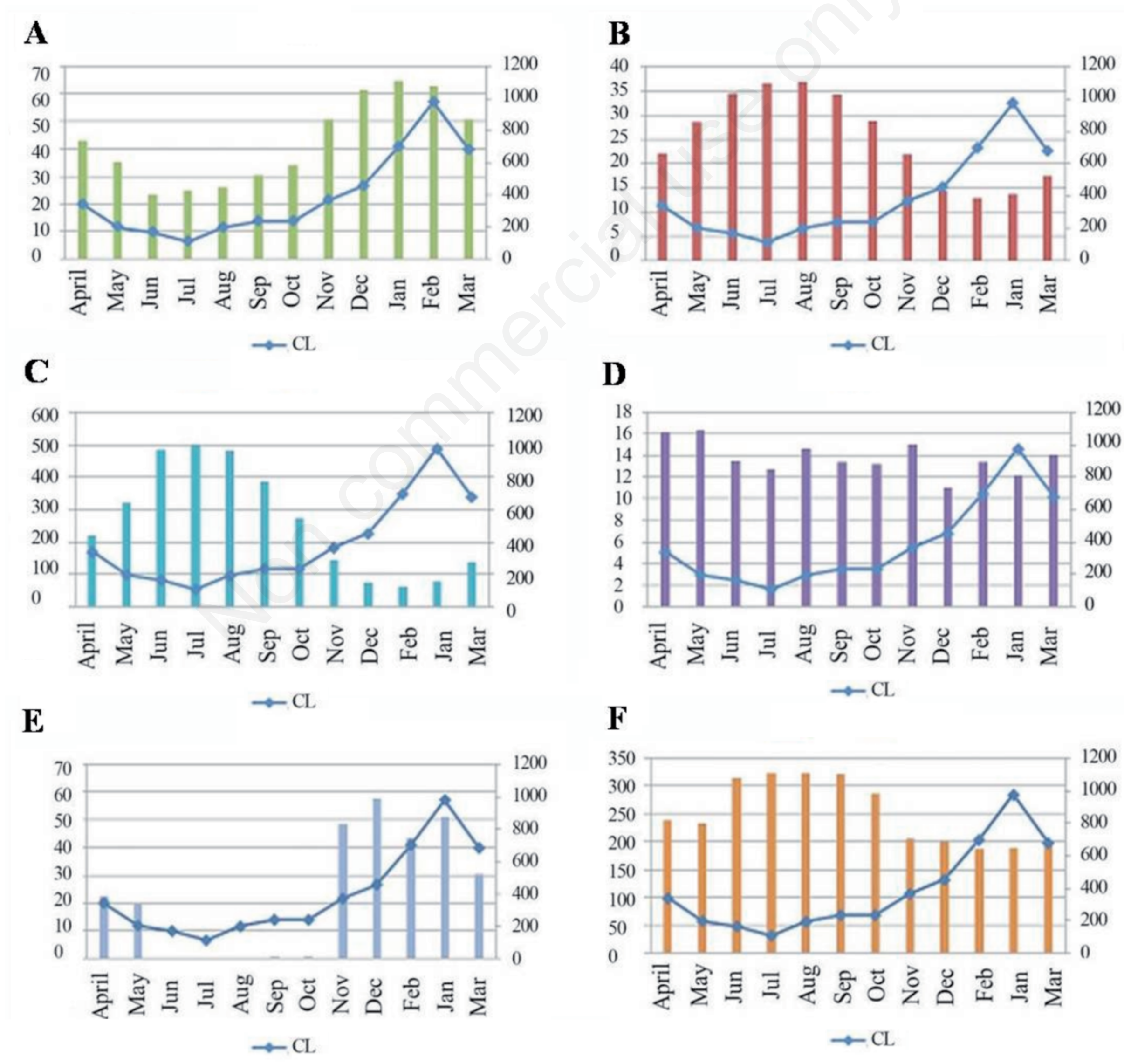

Figure 5. The relationship between the number of patients with cutaneous leishmaniasis and the various variables studied in all districts in the 2010-2014 period: humidity (A), average temperature (B), evaporation (C), wind (D), rainfall (E), sunshine hours (F).

Conclusions

The climatic variability of five recent years in Khuzestan Province may have influenced the epidemiology and transmission of CL. Increase and decrease in the number of the CL patients show that the epidemiologic patterns of CL is changing. The changes in climate including temperature and humidity levels can thus trigger changes in the geographic distribution of leishmaniasis as well as other vector-borne diseases.

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