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# Spatial Analysis and Geographic Factors Associated with Cutaneous Leishmaniasis in Southern Iran

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***ABSTRACT***

***Introduction:*** This study aimed to determine the hotspot areas for Cutaneous Leishmaniasis (CL) in Fasa city and assess the relations between the geographical factors with CL incidence using spatial analysis.

***Materials and Methods:*** This ecological study was conducted in Fasa city, data of the CL disease such as the total number of CL cases and the population at risk from 2009 to 2014. Weather conditions' data including the means of temperature, humidity, rainfall, sunny days, rainy days, and evaporation were collected from the weather forecast centers in Fars province. The disease cases' information such as the number of disease cases was collected from all healthcare centers located in Fasa City. Ordinary Least Square (OLS) and Global Moran's Index (GMI) were used to assess the associations of the various environmental variables with CL incidence and to map clustering of CL cases across the region.

***Results:*** The cumulative incidence of CL was 16 per 10,000 populations during a six-year period. The results showed the southern area of Fasa as a hotspot area which is considered as hyperendemic foci for CL. OLS revealed a high incidence of CL in areas with maximum temperature, mean of temperature, mean of evaporation, sunny days and wind velocity.

***Conclusion:*** A spatial disease pattern was found in the present study. Hence, substantial consideration to environmental data leads to not only suitable protection against CL but also designing a suitable measure for the prevention and control of the disease.

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## Introduction

Leishmaniasis known as a worldwide, zoonotic and vector-borne disease is caused by various *Leishmania* species such as *L. tropica*, *L. major*, *L. donovani*, and *L. infantum* [1] and transmitted by infected female phlebotomine sandflies. The disease is categorized as one of the six important infectious tropical diseases based on the WHO report. Three clinical manifestations of leishmaniasis include cutaneous (CL), visceral (VL), and mucocutaneous leishmaniasis (MCL) involving 22 and 66 countries in Ancient and new

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worlds, respectively [2]. According to the WHO estimate, 700000 to 1 million new cases and also 20000-30000 deaths of the disease arise annually. The highest (87%) rate of CL belonged to the countries including Afghanistan, Algeria, Colombia, Brazil, Iraq, Iran, Tunisia, the Syrian Arab Republic, Yemen and Peru in 2015. Likewise, the majority of CL cases particularly took place in Iran (908 cases) and Turkey (815 cases) [3]. As such, leishmaniasis is considered as a main and unremarkable tropical disease in developing countries such as Iran; therefore, comprehensive global program should be provided to control this zoonotic infection.

Climate changes, environmental, socioeconomic and demographic factors, as well as migration, play the main role in growing the incidence of leishmaniasis [4]. There is a close relationship between the spatial distribution of sand fly vectors and climate change patterns for the incidence of CL [5, 6]. Applying some predicting tools such as Geographic Information System (GIS) is beneficial to analyze spatial data and identify the association between environmental variables including precipitation, humidity, altitude, temperature and distribution of sand flies to design a suitable pattern for the prevention and control of vector-borne diseases such as leishmaniasis as well as regionalizing the climatic factors using kriging method as a spatial correlation modeling [7]. Hence, the goal of the present study was applying GIS for spatial analysis of geographic factors which affect zoonotic CL in Fasa, a notable endemic foci of CL, located in Fars province, Southern Iran.

## Materials and Methods

This ecological study was carried out to investigate geographic factors affecting zoonotic CL.

The place of the study, Fasa city is located in the south of Fars province between 28° 56' 22" North, 53° 39' 0" East (Figure 1). Its altitude from sea level is about 1450m, and the inhabitant population of the city is approximately 200,000 people. The area of this town is 4302km$^2$ space and it is about 145km far from Shiraz, the capital of Fars province, Iran (Figure 1). The average annual temperature is 18.5 °C and the average precipitation is almost 300 mm annually.

**Figure 1:** Map of Iran showing the location of study in Fasa city, southern Iran

### *Data collection*

The geographic information including the averages of high and low temperatures, relative humidity, evaporation, sunshine, wet and icy days, wind direction, wind speed, and rainfall amounts was obtained from the weather bureau of Fars province and Fasa.

Weather conditions' data such as weather information, including the means of temperature, humidity, rainfall, sunny days, rainy days, and

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evaporation were collected from the weather forecast centers in Fars province.

The data of the disease including the incidence of CL and the habited population in various foci of CL occurrence was collected during 2009-2014. The cumulative incidence rate of the CL in 6 years was calculated for each locus.

The disease cases' data including the number of disease cases were also collected from all healthcare centers of Fasa City from 2009 to 2014.

To analyze the climatic data throughout the city, the data were interpolated using the kriging method which was finally popularized to the whole foci. The data were subsequently analyzed by means of ARC GIS 10.2 software.

Akaike Information Criteria (AIC) was also employed in this study in order to choose the best model. The following formulae was used to compute AIC.

$AIC = -2 \times \ln(likelihood) + 2 \times k$

***Statistical methods***

In order to better fit the model, the data were analyzed through the city and foci of the disease. Furthermore, ARC GIS software version 10.2 was applied to spatial analysis and to assess the relationship between climatic variables and CL. Spatial models such as geographically weighted regression (GWR) and ordinary least square (OLS) were considered for 12 climatic variables (Table 1). However, owing to the high correlation between variables, GWR was not found as a functional model and the OLS model was used instead following the correlation test between residuals (spatial autocorrelation (morans) residual). The statistical significant coefficient for OLS and Robust probability (Robust-Pr) models was considered as a p-value < 0.01 level. The total fitness of the model for chi-square of joint Wald statistic and chi-square of joint F-statistic was also defined as $p < 0.01$.

**Table 1:** Description of explanatory variables in the study

| Variable | Mean ± SD | Minimum | Maximum |
|---|---|---|---|
| Years of assembling leishmaniasis cases | | | |
| 2009 | 1.62 ± 9.78 | 0 | 159 |
| 2010 | 0.86 ± 3.18 | 0 | 30 |
| 2011 | 1.03 ± 8.51 | 0 | 38 |
| 2012 | 1.63 ± 8.88 | 0 | 120 |
| 2013 | 1.07 ± 6.75 | 0 | 100 |
| 2014 | 0.88 ± 3.52 | 0 | 38 |
| Cumulative incidence of CL in 6 years | 16 ± 59 | 0 | 584 |
| Ecology variable | | | |
| Minimum temperature | 6.55 ± 1.09 | 4.91 | 8.66 |
| Maximum temperature | 21.5 ± 0.5 | 20.81 | 22.9 |
| Mean temperature | 14.03 ± 0.8 | 12.81 | 15.75 |
| Minimum relative humidity | 22.36 ± 0.37 | 21.91 | 22.73 |
| Maximum relative humidity | 55.98 ± 0.59 | 55.22 | 56.8 |
| Mean relative humidity | 39.2 ± 0.43 | 38.7 | 39.81 |
| Average rainfall | 289.61± 6.37 | 281.88 | 299.15 |
| Total rainy day | 42.91 ± 1.11 | 41.15 | 44.83 |
| Mean of Evaporation | 122.55 ± 6.38 | 110.06 | 131.02 |
| Sunny days | 137.33 ± 8.52 | 163.04 | 189.5 |
| Freeze days | 81.98 ± 14.3 | 52.95 | 101.87 |
| Direct wind | 226.6 ± 4.35 | 221.32 | 232.96 |
| Wind velocity | 15.33 ± 0.28 | 14.56 | 15.63 |

## Ethical issues

This study was approved by the Medical Ethics Committee of Fasa University of Medical Sciences No: IR.FUMS.REC.1396.315

## Results

Table 1 shows the data of disease cases in Fasa from 2009 to 2014, it also shows the cumulative incidence of CL in 6 years and climatic variables



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in these regions. According to the results, the average rate of the total incidence of CL in 6 years was calculated as 59 ± 16 in 10,000 people. Figure 2 presents the pattern of a hot spot with 90-95% confidence interval for the disease, in which red points were positioned in the south spaces of Fasa, indicate a high rate of the disease and are considered as hyperendemic foci of CL. However, the majority of the disease (60%) belonged to the children under 10 years old.

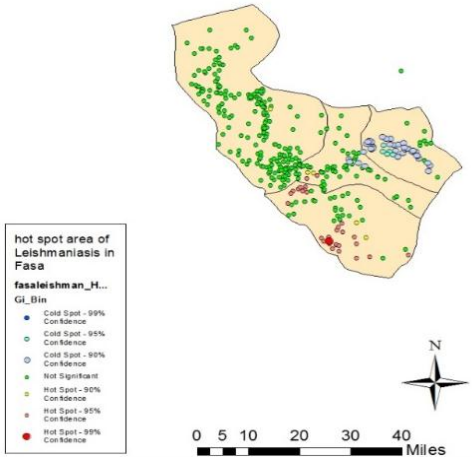


**Figure 2:** Hot spot areas of Leishmaniasis in Fasa, Southern Iran during 2004-2014 (Incidence rate per 10,000 cases)

The results extracted from the OLS model showed direct and indirect associations of the various variables and their averages with CL incidence respectively ($p < 0.01$) (Table 2). Moreover, the chi-square of joint wald statistic was considered as 24.18 with P = 0.029 and chi-square of joint F-statistic was also used as 2.01 with p = 0.019 for analyzing the fitness model of OLS. Details are demonstrated in Table 3.

Spatial autocorrelation (Moran's I) residual index indicated a lack of correlation between residuals and showed model fitness (p = 0.975) (Table 4) (Figure 3).

**Table 2:** Summary of ordinary least square (OLS) results – Model variables

| Variable | Coefficient [a] | Standard Error | Probability [b] | Robust_t | Robust_Pr [b] |
|---|---|---|---|---|---|
| Intercept | -9117.18 | 10378.9 | 0.38 | -1.17 | 0.24 |
| Minimum temperature (°C) | 3615.63 | 1354.01 | 0.08* | 2.40 | 0.02 |
| Maximum temperature (°C) | 3995.75 | 1405.07 | 0.005* | 3.33 | 0.001 |
| Mean of temperature (°C) | -7491.98 | 2574.57 | 0.004* | -3.06 | 0.002 |
| Minimum relative humidity (%) | 2519.90 | 1431.34 | 0.08 | 2.77 | 0.006 |
| Maximum relative humidity (%) | 1326.45 | 1213.49 | 0.27 | 1.63 | 0.103 |
| Mean of relative humidity (%) | -3471.26 | 2468.04 | 0.16 | -2.14 | 0.033 |
| Mean of rainfall (mm/d) | -29.56 | 23.60 | 0.21 | -1.36 | 0.17 |
| Mean of rainy days (mm/d) | 26.77 | 83.60 | 0.75 | 0.30 | 0.77 |
| Mean of evaporation (mm/d) | 38.27 | 16.42 | 0.02* | 2.44 | 0.015 |
| Sunny days (%) | -23.91 | 10.95 | 0.03* | -2.00 | 0.046 |
| Wind velocity (m/h) | 682.65 | 287.64 | 0.02* | 2.43 | 0.015 |

(*) An asterisk indicates a statistically significant p-value ($p < 0.01$).
[a] Coefficient: Represents the strength and type of association between each explanatory variable and the dependent variable.
[b] Probability and robust probability (Robust-Pr): Asterisk (*) indicates a statistically significant coefficient ($p < 0.01$).

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**Table 3:** Report of ordinary least square (OLS) diagnostics

| Number of observations | Multiple R-Squared [D] | Joint F-statistic [E] | Joint wald statistic [E] | Akaike`s Information Criterion (AICc) [D] | Adjusted R-Squared [D] | Prob ( > F), (13,363) degrees of freedom | Prob ( > Chi-squared), (13) degrees of freedom |
|---|---|---|---|---|---|---|---|
| 377 | 0.067 | 2.01 | 24.18 | 4149.85 | 0.034 | 0.019* | 0.029* |

[a] R-Squared and Akaike's Information Criterion (AICc): measures of model fit/performance.
[e] Joint F and Wald statistics: Asterisk (*) indicates statistically significant p-value for the model (p < 0.01).

**Table 4:** Correlation test between residuals

| Spatial autocorrelation (morans) residual | |
|---|---|
| Index | - 0.00146 |
| Z score | 0.030087 |
| p-value | 0.975 |

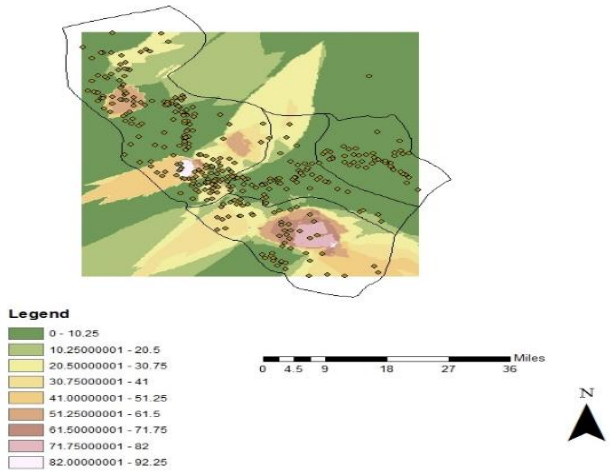


**Figure 3:** Predicted projection of leishmaniasis incidence using all explanatory variables interpolated in OLS model

## Discussion

Distribution patterns of vector-borne diseases are widely affected by environmental conditions and climate factors especially temperature [7-9]. The significant effect of climate variability on leishmaniasis has been confirmed in South America, and the Eastern Mediterranean area [8, 10, 11]. Recent advances in scientific literature and technology such as GIS have developed the availability of predicting and recognizing environmental data including climate change, ecology, topographic maps and their effects on diseases such as leishmaniasis distribution correlated with the environmental factors [7, 12, 13].

As known, Fars province is found as a substantial focal of leishmaniasis, where the incidence rate of CL has been highly grown in recent years. Zare et al. studied on CL patients in Fars province using spatiotemporal cluster analysis from 2010 to 2015. According to their result, Fasa was categorized in the largest cluster (60% of all cases) among the six clusters [14]. The expanded distribution of sand flies in various areas of Fars province has increased the potency of CL incidence [14, 15].

Previous reports showed significant spatial distribution between the prominent eco-environmental factors including precipitation, maximum relative humidity, minimum temperature, wind velocity and CL incidence using various predictor models. Therefore, the results of



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the present study are consistent with other publications [5, 8, 14, 16].

In the present study, the spatial distribution of the disease showed a significant direct correlation with maximum and minimum temperature, although the diverse correlation was found with the average temperature. Moreover, minimum and average relative humidity showed a direct and adverse correlation with the spatial distribution of CL, respectively. The results are similar to the former report revealed in Tunisia [17].

Sunny days had also indirect correlation while wind velocity and the average of evaporation showed a significant direct correlation with the spatial distribution of the disease. Based on the results, temperature and relative humidity were introduced as the main predictors which were similar to the previous study done in Iran [9]. These environmental factors may provide the vector (*Phlebotomus papatasi*) and the reservoir (*Rhombomys opimus*) for increasing the incidence of CL in Fasa region.

It should be considered that the climatic information evaluated in the current study was only a part of risk factors influenced by the disease. Other determinant factors such as socioeconomic agents may play an effective role on CL incidence in Fasa country which is not included in this study. Furthermore, some limitations affected the results for example, due to the passive surveillance system of CL in Iran, many patients may not be comprised estimating of the disease. Also, vectors and reservoir variables were not included in the research and weather information was only collected from one weather station.

## Conclusion

The substantial consideration to environmental data leads to not only suitable protection against CL but also designing a suitable measure for the prevention and control of the disease which is predicted by spatial analyzing methods such as GIS.

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## Conflict of interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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