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Spatial modeling of visceral leishmaniasis in Iran from 2010 to 2018

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Abstract---Kala-Azar is the most lethal type of leishmaniasis, sporadic in most parts of Iran and prevalent in some provinces. Using the Geographical Information System (GIS) and satellite data analysis, we intended to assess the disease's incidence in Iran. Methods: Using GIS, data received from the Ministry of Health and Medical Education in Tehran, Iran, and other associated institutions between 2010 and 2018 were evaluated. The disease's geographical distribution maps were then constructed, and the disease's hotspots in Iran were identified using spatial analysis using ArcGIS10.5 software. Geographically weighted regression (GWR) analysis in ArcGIS10.5 was used to link disease-influencing variables such as temperature, relative humidity, normalized difference vegetation index (NDVI), and incidence of visceral leishmaniasis. Linear regression analysis, SPSS 21 software descriptive statistics, and chi-square test were used to analyze the data. Results: This study revealed that the provinces of Ardabil, East Azarbaijan, North Khorasan, and Fars were the hot spots of VL. The provinces of Ardabil, East Azarbaijan, North Khorasan, Fars, Bushehr, Semnan, Sistan, Baluchistan, Esfahan, Chaharmahal Bakhtiari, Qom, Golestan, and Kerman had the highest correlation between temperature, vegetation density, and the incidence of Kala Azar, as determined by geographical weighted regression analysis. Conclusion: The use of maps might give accurate estimates of populations at risk. The probability of the presence of visceral leishmaniasis in an area was more influenced by climatic conditions such as temperature, humidity, and NDVI. These indicators can help as a predictor of the occurrence of disease. Visceral leishmaniasis is linked to environmental and climatic conditions.

Keywords---*Leishmaniasis Visceral, Incidence; Geographical information system, Environmental variable Iran.*

Introduction

Leishmaniasis is a severe international public health problem that is reemerging and is one of the most neglected tropical diseases. The most serious form of leishmaniasis in Iran is zoonotic visceral, or Kala-azar (ZVL), the most lethal and severe form of this disease. This disease can distribute to new places as a result of the influence of environmental variables (1-4). The majority of ZVL cases (92.8%) were reported in children under the age of 12 years (5). This disease has a worldwide prevalence of 12–14 million cases and an annual incidence of 1.5–2 million cases. Each year, around 500,000 new cases of VL are reported globally. More than 350 million people living in high-risk areas were exposed to various leishmaniases, according to WHO reports. According to official reports, there were 59,000 VL-related deaths annually. (6). In global studies of leishmaniasis disease, climatic conditions (temperature, rainfall, humidity, etc.) and terrain features (vegetation, land height above sea level, earthquake proneness, etc.) are the two most important environmental factors associated with the presence of this disease (7). Currently, a Geographic Information System (GIS) is utilized to map the geographical distributions of disease prevalence, factors that influence the transmission and control of disease, and the spatial modeling of environmental factors that have actual effects on disease occurrences (5, 8-11). At present, a Geographic Information System (GIS) is used to map the geographical distributions of disease prevalence, variables that impact the transmission and control of disease, and the spatial modeling of environmental factors that have real effects on disease occurrences (12). We aim to evaluate the incidence, regional distribution, and hotspots of Visceral Leishmaniasis (VL) in Iran from 2009 to 2018 using a Geographic Information System.

Methods

Data gathering The Ministry of Health (Disease Management Center), Tehran, Iran, articles released about the disease in the country, and in-person visits to select related provincial centers were used to collect data on VL in all provinces of Iran from 2010 to 2018. Searching for conference abstracts and dissertation abstracts was an additional source of information. We acquired information on the country's population from the Statistics Center of Iran. (13). From 2010 to 2018, nine-year meteorological data were gathered from climatological stations in the country's 31 provinces. these data were about yearly temperatures and relative humidity from the National Meteorological Organization. The average annual temperature and relative humidity were computed for each province's meteorological stations, and then for each province, they were averaged to provide one temperature and one humidity Value for the study. Using the Google Earth Engine software, we obtained the NDVI layer based on the Iranian border for May from 2010 to 2018 with a spatial resolution of one square kilometer per pixel. These layers were clipped in ArcMap based on the borders of the provinces of the country and the average value of NDVI for different years in each province was calculated. The obtained numbers were used for geographical weighted regression in ArcMap10.5. For data analysis, the following formula was used to calculate the incidence rate per 100,000 people in the province's population: Incidence rate = (new disease cases) / (risk in the population) × 100000

Spatial analysis

ArcMap was used to generate a spatial database of the disease that includes patients' age, mortality, location, and gender in different age groups. Then, spatial distribution maps of the disease were produced from 2010 to 2018. Using spatial analysis of ArcGIS 10.5 software and the Hot Spot Analysis tool, the disease's hot spots were determined in Iran's provinces. Hot Spot Analysis in ArcGIS software is a method for finding provinces with significantly different disease incidences from other provinces. This database analysis based on disease provides positive and negative Z-scores for each province. It shows which provinces have significantly more disease hotspots and which have fewer. The greater the positive value of Z-scores, the more critical the points, whereas the greater the negative value, the less critical the points. After doing the analysis, the points are classified into groups of hot and cold points at three confidence levels: 90%, 95%, and 99%, and each category has its own Z-value. During 2009–2018, spatial analysis of geographically weighted regression in ArcGIS 10.5 was used to study the relationship between environmental factors that affect the disease, such as temperature, relative humidity, and NDVI density, and the incidence of Kala Azar.

We used geographically weighted regression (GWR) analysis to model spatially the relationship between the number of cases of visceral leishmaniasis during the study period, which was the dependent variable, and the average annual temperature, average annual relative humidity, and NDVI, which were the independent variables. (14, 15) Statistical analysis of the data was performed using linear regression analysis and SPSS 21 software (Chicago, IL, USA) using descriptive statistics and a chi-square test.

Results

658 cases of visceral leishmaniasis were reported in the country during the study years. Figure 1 shows the incidence rate of visceral leishmaniasis. During nine years, the provinces of Ardabil, East Azarbaijan, North Khorasan and Fars had the highest rate of Visceral leishmaniasis (Fig. 2). The hot spots of the disease, i.e., the provinces with the highest rate of incidence of visceral leishmaniasis, were Ardabil, East Azarbaijan, North Khorasan, and Fars (Fig. 6). Moreover, the GWR analysis revealed that throughout these years, the association between humidity (Fig. 3), temperature (Fig. 4) and NDVI (Fig. 5) was the highest. and the incidence of the disease was observed in the provinces of Ardabil, East Azarbaijan, North Khorasan, Fars, Bushehr, Semnan, Sistan, Baluchestan, Esfahan, Chaharmahal Bakhtiari, Qom, Golestan, and Kerman. Data analysis revealed that there were 66 new instances of visceral leishmaniasis in 2018. The incidence of VL was 0.1 per 100,000 patients on average. According to these statistics, the highest number of new cases of visceral leishmaniasis was in 2012 (1104 cases). The lowest number of new cases of VL was estimated in 2014 (55 cases). The association between the incidence of visceral leishmaniasis in 100,000 patients, normalized difference vegetation index (NDVI), relative humidity (RH), and mean temperature (TM) was analyzed using linear regression (Table 1). There was no significant correlation between temperature (TM), Normalized difference vegetation index (NDVI), relative humidity (RH), and the incidence of Visceral leishmaniasis, according to the results of the analysis (Table 2).

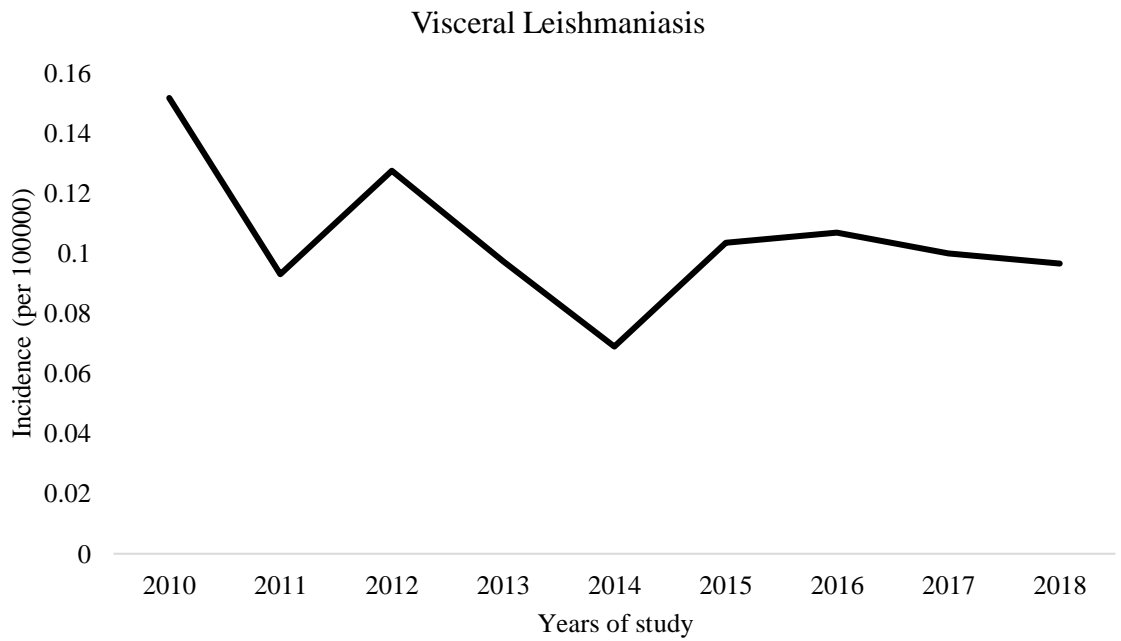


Fig. 1: The trend of Visceral leishmaniasis during the years 2010-2018 in Iran

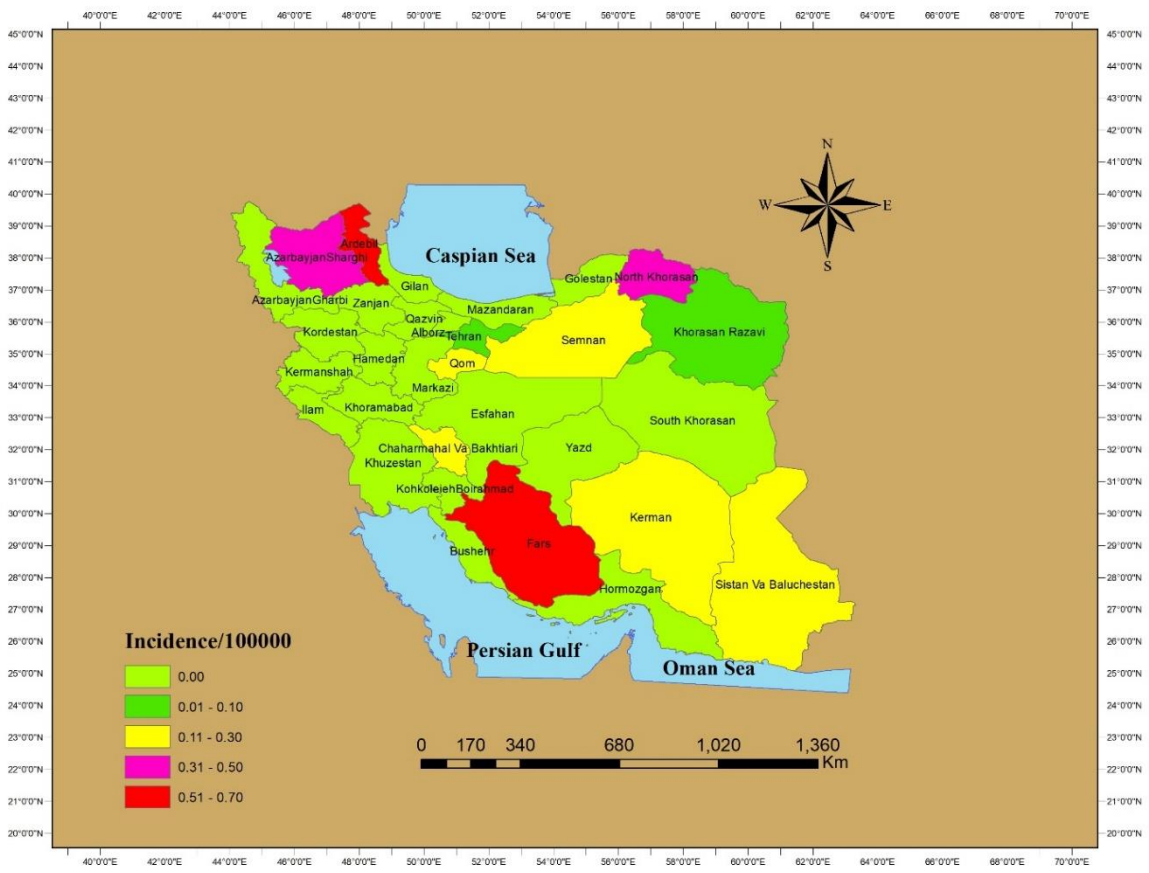


Fig. 2: The incidence of Visceral leishmaniasis in different provinces of Iran, 2010-2018

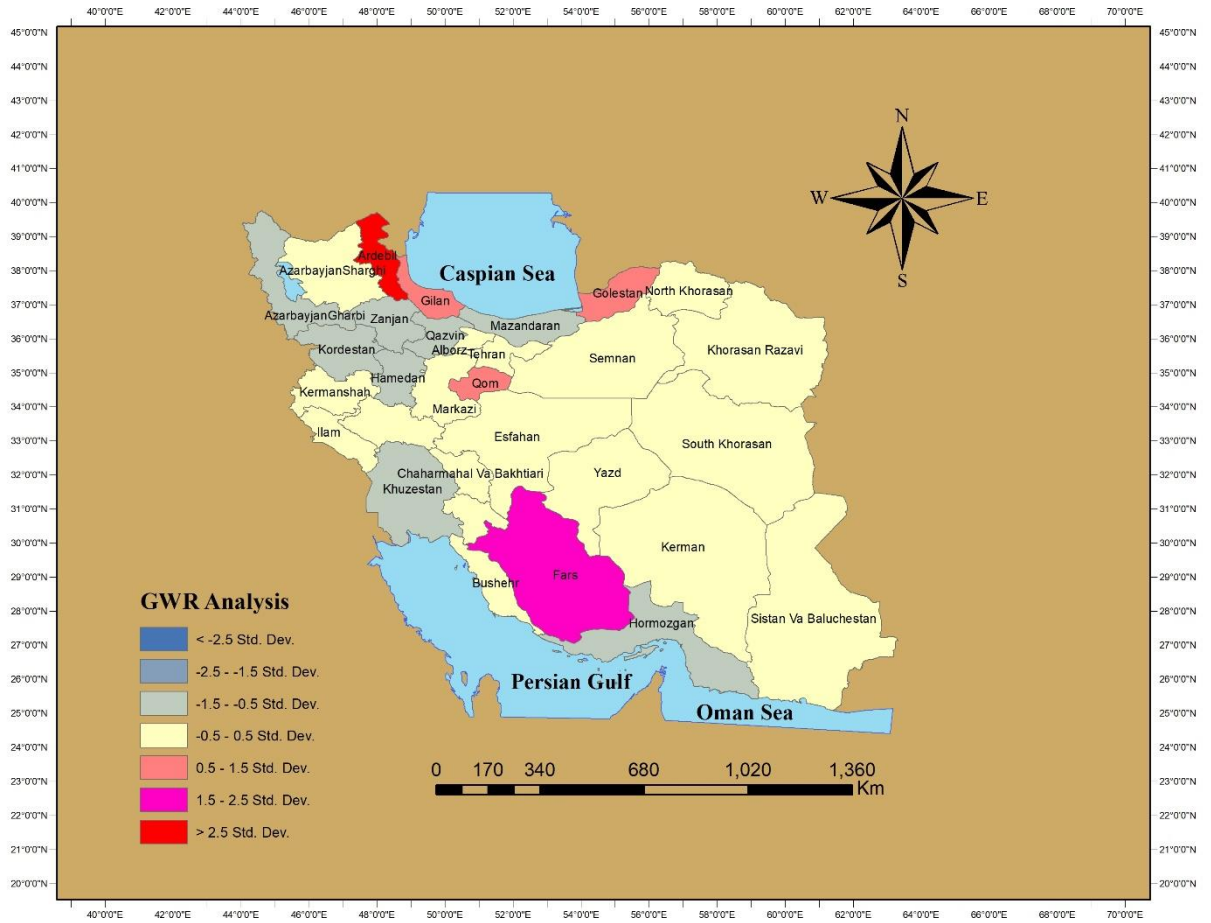


Fig. 3: The results of geographically weighted regression analysis of the correlation between the relative humidity and the incidence of Visceral leishmaniasis in Iran, 2010-2018

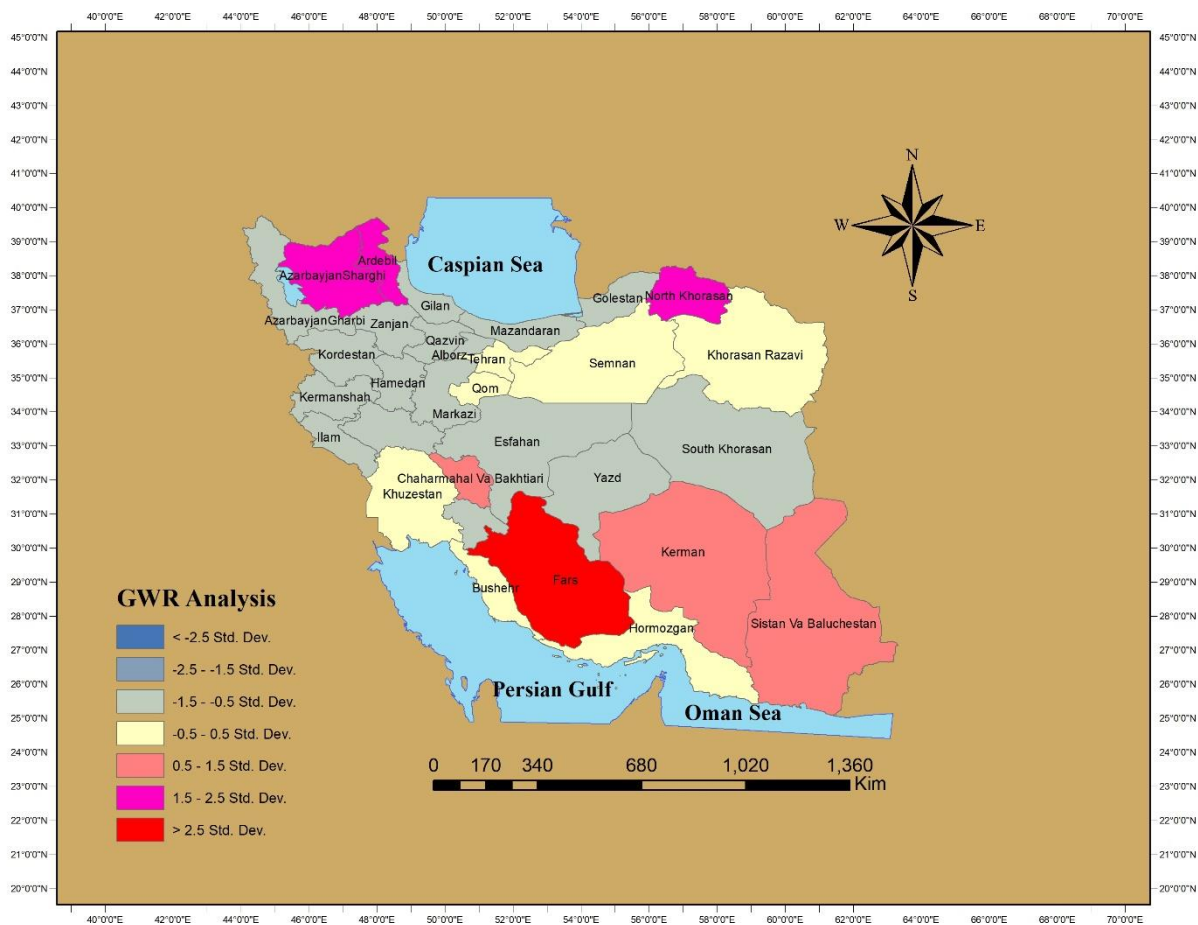


Fig. 4: The results of geographically weighted regression analysis of the correlation between the temperature and the incidence of Visceral leishmaniasis in Iran, 2010-2018

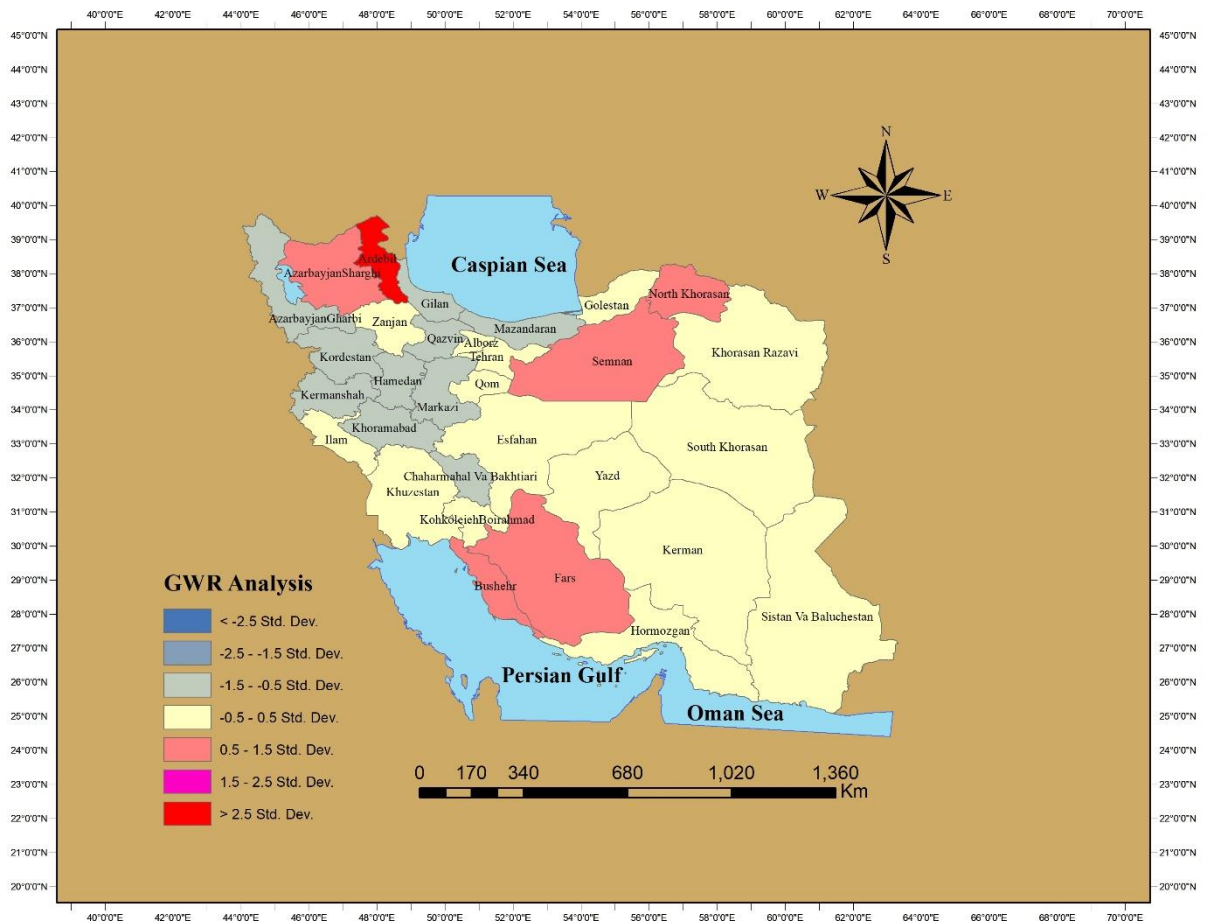


Fig. 5: The results of geographically weighted regression analysis of the correlation between NDVI and the incidence of Visceral leishmaniasis in Iran, 2010-2018



Fig. 6: The Hotspot Visceral leishmaniasis in different provinces of Iran, 2010-2018

Table 1: Relationship between environmental variables and the incidence of Visceral leishmaniasis in Iran, 2010-2018

province	TM	RH	NDVI	Incidence/100000
Alborz	16.33376905	43.45	0.2	0.01
Ardebil	9.239111554	68.83333333	0.3	0.8
AzarbayjanGharbi	13.60242297	58.11111111	0.3	0
AzarbayjanSharghi	12.79792522	51.22222222	0.3	0.3
Bushehr	25.51700331	63.88888889	0.1	0.2
Chaharmahal Va Bakhtiari	12.55272017	44.38888889	0.2	0.1
Esfahan	14.05331549	37.44444444	0.1	0.03
Fars	17.55483554	38.77777778	0.1	0.4
Gilan	15.93664585	77	0.6	0.07
Golestan	18.56516723	42.38888889	0.4	0.09
Hamedan	9.995986178	49.72222222	0.3	0.03
Hormozgan	24.452925	62.5	0.08	0.04
Ilam	20.32158667	41.16666667	0.1	0
Kerman	24.43620325	46.27777778	0.1	0.07
Kermanshah	15.61526863	34.22222222	0.3	0.02
Khorasan Razavi	15.10083742	66.33333333	0.1	0.02
Khuzestan	25.07962542	44.5	0.1	0.01
Kordestan	12.97535104	47.72222222	0.4	0
Markazi	12.282844	43.38888889	0.2	0.01
Mazandaran	16.30767715	76.33333333	0.5	0.01
North Khorasan	14.74743672	57.72222222	0.2	0.05
Qazvin	15.29310111	52.88888889	0.3	0.02
Qom	16.29953661	44.77777778	0.1	0.07
Semnan	15.4222297	37.55555556	0.08	0.01
Sistan Va Baluchestan	23.27281388	29.38888889	0.07	0.06
South Khorasan	18.52849936	33	0.08	0
Tehran	15.85840555	36.22222222	0.2	0.03
Yazd	17.50630777	36.22222222	0.08	0
Zanjan	12.97596834	54.38888889	0.3	0.02

TM: Mean annual temperature, RH: Average of annual relative humidity, NDVI: Normalized difference vegetation index.

Table 2: Results of the univariate and multiple linear regression model for Visceral Leishmaniasis

variable	univariate		multiple	
	Beta(SE)	P-value	Beta(SE)	P-value
TM	-0.008(0.007)	0.248	-0.011(0.008)	0.172
RH	0.003(0.002)	0.179	0.005(0.003)	0.117
NDVI	0.075(0.227)	0.745	-0.316(0.293)	0.291

TM: Temperature, RH: Average of annual relative humidity, NDVI: Normalized difference vegetation index

Discussion

The most significant achievements of this study are maps based on accurate data for the spread of visceral leishmaniasis in Iran, in addition to the identification of detailed variables of environmental factors influencing disease distribution. In these maps, the disease condition in Iran might be correctly described because it includes all of the scientific information collected by experts over decades. In this study, the hot foci of visceral leishmaniasis were estimated using spatial analysis. During 2010-2018, cold foci of the disease, i.e., provinces in which the incidence of the disease was significantly low, were not observed. In addition, GWR was used to correlate the variables affecting the disease. Though the normalized difference vegetation index, annual temperature, and annual relative humidity have a statistically (GWR) significant relationship with the incidence of visceral leishmaniasis, this study (especially for simple linear regression models) implies a complex and indirect relationship. The results of this investigation are close to a recent study in Iran.(16, 17) Several studies in India(18, 19) , and Brazil(20) have demonstrated significant associations between disease incidence and temperature. In different regions of the world, research has been performed in an effort to have a better knowledge of the ecology of VL. For example, (21) The results demonstrated the significance of Brazil's low normalized difference vegetation index (NDVI) on the frequency of both human and canine VL. These conclusions are supported by observations made in the northern region of India. (22) Our data indicate that Mediterranean visceral leishmaniasis is distributed differently in different geographical areas of Iran. Using spatially weighted regression analysis, the link between temperature, relative humidity, NDVI, and the prevalence of human visceral leishmaniasis was studied in this study. Ardabil, East Azarbaijan, North Khorasan, Fars, Bushehr, Semnan, Sistan, Baluchestan, Esfahan, Chaharmahal Bakhtiari, Qom, Golestan, and Kerman province. The highest correlation was observed between temperature, relative humidity, and NDVI with the incidence of visceral leishmaniasis, which is similar to other studies. (16, 23-27). The results of Danson et al. The study demonstrated that the application of GIS to the study of human parasitic diseases is highly beneficial and shows a deeper understanding of parasite transmission. It demonstrated that environmental parameters including temperature, humidity, and altitude influence the transmission of parasitic diseases.(28) which is in accordance with our findings. Therefore, it may be inferred that leishmaniasis is climate-sensitive. Changes in temperature, humidity, and other environmental conditions influence its epidemiology due to its effects on population numbers, In addition, these parameters have a considerable impact on the distribution of the main reservoir species.(29) A study of environmental factors influencing the spread of vectors in north-eastern Italy distribution, growth, and sandfly survival.(30, 31) indicated that regions with high winter NDVI may be associated with the survival of larvae in moist environments.(32) . Studies of *L. infantum* infection frequency in dogs according to different regions of the country show that it was distributed mainly in 20 provinces of Iran, Ardabil, Bushehr, East Azarbaijan, Razavi Khorasan, Chaharmahal and Bakhtiari, Isfahan, Fars, Qom, Golestan, Kerman, Khuzestan, Kohgiluyeh and BoyerAhmad, Mazandaran, North Khorasan, Semnan, Sistan, and Baluchestan, this disease exist.(33) .Consequently, it seems to be inferred that dogs and wild canines are the most significant reservoirs of *L. infantum* in the old and new worlds. (23, 34). In Iran,

high canine infection rates should be regarded as the most significant risk factor for VL. (24, 35-37) (6, 12-14, 49). Due to the large dog population, it appears that the number of infected dogs in each area has the highest potential for transmission of disease. Therefore, it is possible to claim that environmental variables had the greatest impact on the Old World distribution of leishmaniasis. (38) The distribution of VL in Fars Province is affected by a mixture of ecological and nomad demographic factors, according to information accessible in the country. However, the most important criteria are being close to the NTR and the role of nomads in the transmission and continuance of Kala-Azar. (26). Concerning the influence of population immigration on the distribution and occurrence of new or reemerging leishmaniasis diseases, several studies have been conducted. (39-41) Nowadays many nomadic people have abandoned their nomadic lifestyle for a rural or urban existence. In towns and cities, there are relatives of emigrating nomads who have close links with them and thus contribute to the maintenance of the disease in these areas. All of the above situations have turned nomads into a population at high risk for kala-Azar, resulting in the stability of VL in Iran's southwest foci. (26) Similar to what happened in North America, agricultural fields may become breeding grounds for sand flies. Also, forests with deciduous trees create suitable conditions for the reproduction of sand flies. (42) Moreover, sparse jungles are residences to canidae family animals, such as foxes, wolves, and jackals, which sometimes visit nearby farms, gardens, and suburban areas in search of food. (14). Leishmaniasis and Kala-Azar disease are prevalent in rural areas with abundant livestock-related vocations and high child-to-dog contact. (43)

Consequently, deforestation, climatic change, the movement of nomads, and the availability and diversity of animal carriers and reservoirs (including jackals) are among the likely causes associated with the increase in the incidence of visceral leishmaniasis in Iranian districts. Individual factors such as genetics, malnutrition, and a weak immune system can also create the ground for infection with this disease. (44, 45) In addition to environmental factors, human activities that increase exposure to sandflies and the presence of animals, such as dogs, that facilitate the *Leishmania* life cycle play crucial roles in the development of visceral leishmaniasis.

Conclusion

The spatial regression model can produce reliable results in predicting VL cases in Iran. Health policymakers can use the data obtained in these methods to prevent the increase of new cases. Therefore, educating people to avoid new cases, screening existing patients who may be disease reservoirs, and treating them in endemic areas, considering factors such as weather conditions and other environmental elements in programs such as Control will be beneficial.

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