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A COMPARISON OF BIOCLIMATIC FACTORS EFFECT FOR CUTANEOUS LEISHMANIASIS CURRENT STATUS BETWEEN EASTERN MEDITERRANEAN REGION AND TIGRIS BASIN OF TURKEY BY USING ECOLOGICAL NICHE MODELING

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Abstract

Cutaneous leishmaniasis (CL) is known as tropical and subtropical neglected vector-borne disease in the Old World. Despite the fact that the Eastern Mediterranean Region and Tigris Basin are an endemic area of CL, unfortunately their bio-climatic and environmental variables are relatively poorly understood.

The aim of the present study were determining the distribution of disease intwo endemic foci and comparison of variables in terms of CL epidemiology. For this purpose, extracted numbers of environmental variables from different sources and determined 3044 CL cases' location information obtained from the ministry of health database to are used for modeling of the CL current probability of occurrence. The ecological niche model (ENM) analysis was used for this purpose. ENM analyses are made by using ArcGIS and MaxEnt softwares to explore the ecological conditions of the disease. Our results emphasized that CL current the area under the curve (AUC) value were found 0.868, 0.918 and 0.924 in Adana, Mersin (East Mediterranean Region) and Diyarbakir (Tigris Basin) respectively. Also, BIO1, BIO4, BIO5, BIO9, BIO10 and DEM were found related to the presence of native human cases of CL in East Mediterranean Region. BI O2, BIO4 and BIO11 were found to correlate with CL probable distribution in Tigris Basin. Consequently, there were relationship between temperature data and disease epidemiology for both areas. Also, comparison results of the study could be a reference to the health ministry's CL and vector control studies

***Key words**: cutaneous leishmaniasis**,** ecological niche modeling, MaxENT, bioclimatic factors, Eastern Mediterranean Region, Tigris Basin.*

INTRODUCTION

All clinical types of leishmaniases are vector-borne diseases caused by parasites protozoan from the genus *Leishmania* (Trypanosomatida: Trypanosomatidae). Accordance with the leishmaniases epidemiology information; reported in large areas of the tropics, sub-tropics, and the Mediterranean basin, including more than 98 countries, where there are a total of 350 million people at risk and 12 million cases of infection.

Leishmaniasis presented two clinical forms in Turkey:

- Visceral leishmaniasis (VL), the most severe and fatal in almost all cases (if is left untreated),
- Cutaneous leishmaniasis (CL) which has a tendency towards spontaneous resolution (Ok et al., 2002; Singh, 2004).

There were two well-known CL high endemic foci in Turkey caused two different *Leishmania* Ross, 1903 (Kinetoplastida: Trypanosomatida) species. *Leishmania infantum* Nicolle, 1908 (Kinetoplastida: Trypanosomatida) is responsible for both clinical forms occurred many cities of the Mediterranean Region (Mainly Adana, Antalya and Mersin) while *Leishmania tropica* Wright (Kinetoplastida: Trypanosomatidae) causes CL in Tigris Basin (Mainly Diyarbakir and Sanliurfa) of Turkey (Ok et al., 2002). *L. infantum* and *L. tropica* transmitted by dominant species *Phlebotomus tobbi* Adler & Theodor (Diptera: Psychodidae) and *Phlebotomus sergenti* Parrot, respectively in two focused endemic region (Alptekin et al., 1999; Simsek et al., 2007; Svobodova et al., 2009; Kavur & Artun, 2017).

46.003 new cases were reported in our country between 1990 and 2010. 96% of these cases were reported from Şanlıurfa, Adana, Osmaniye, Hatay, Diyarbakir, Icel and Kahramanmaras provinces (Sucakli & Saka 2007; Gurel et al., 2012).

Related environmental data obtained from different sources have been used for the analyzing of infectious diseases predicted epidemiology by using geographic information systems technologies (Ostfeld et al., 2005). Ecological niche models (ENM) investigations carried out with basic and powerful computers could be used for estimation modeling of various species distributions, environmental requirements, epidemiological status of some neglected diseases (Ostfeld et al., 2005; Philips 2006). Also ENM, including maximum entropy (MaxEnt) present-only data, is widely used in ecology and biodiversity conservation in modeling species distribution and diseases such as malaria and leishmaniasis (Elith et al., 2006).

The aim of this study, comparison of CL current status between Mediterranean Region and Tigris Basin, specifically selected foci in terms of bioclimatic factors and patients report number and locations using MaxENT and ArcGIS software.

MATERIALS AND METHODS

Study Area

We selected three endemic foci (Mersin, Adana and Diyarbakir) in two geographical regions, because of the high number of CL patients reported before.

Mersin is Turkey's 11th major city and it is located in the Eastern part of the Mediterranean Region. Mersin's basin is 15.853 km^2 in area. The South and North aspect of Mersin are Mediterranean sea and East Taurus Mountains, respectively.

Also, Mersin has 13 districts and its altitude is 100 m. It is located at 36°48'43.575" north latitude and 34°38'29.331"east longitude. Mersin has a population of 1.814.468 according to the latest population data in 2018 (TSI 2018) (Figure 1).

Adana is locatedin the eastern part of the Mediterranean Region of Turkey andit is the fifth major city of Turkey. The city has a human population of 2.220.125. Its basin is 14,032 km^2 in area. Adana has fifteen districts and it is located at 37.002 latitude and 35.329 longitude (UTM Zone 36N - WGS84)(TSI, 2018) (Figure 1).

Diyarbakir is the 12th largest city in Turkey, is located in the Northern part of the Tigris Basin. Its basin is 15168 km^2 and generally surrounded by mountains.

The central part of Diyarbakir is slightly pitted and is surrounded by the tributaries of the Southeastern Taurus. Diyarbakır, which has 17 districts, has a height of 674 m. The city of Diyarbakır is located at 37°54'39" North latitude and 40°14'12" East longitude. As of the end of 2018, its population is 1.732.396 (TSI, 2018) (Figure 2).

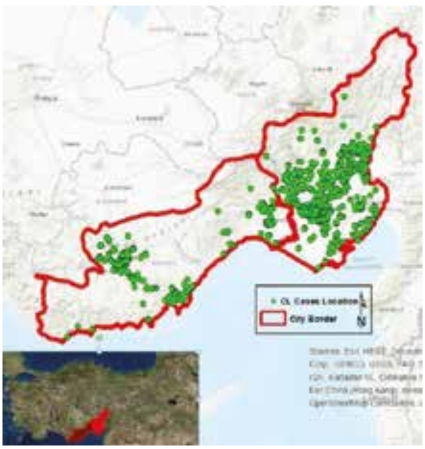

Figure 1. CL cases location and study areas of East Mediterranean Region (Adana and Mersin Province)

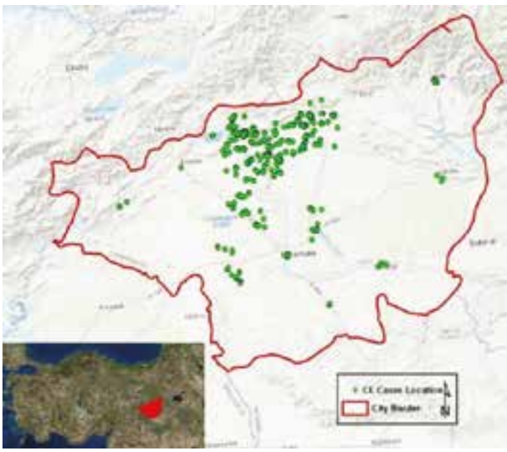

Figure 2. CL cases location and study areas of Tigris Basin (Diyarbakir Province)

Bioclimatic and Environmental Parameters
The environmental data included three variables derived from remotely sensed data and 19 bioclimatic (bioclim) variables (Table 1). The current variables were downloaded from WorldClim website, version 1.416. The bioclimatic variables all had a nominal resolution of approximately 1 km^2. The current data were developed from monthly average climate data between 1950 and 2000 using observed data. The current bioclimatic variables describe the climatic conditions such as temperature, isothermality, annual precipitation.

Table 1. Bioclimatic and environmental data

Name of Data	Description
BIO1	Annual mean temperature (°C)
BIO2	Mean diurnal range [mean of monthly (max temp - min temp)] (°C)
BIO3	Isothermality (BIO2/BIO7) (x100)
BIO4	Temperature seasonality (standard deviation x100)
BIO5	Max temperature of warmest month (°C)
BIO6	Min temperature of coldest month (°C)
BIO7	Temperature annual range (BIO5-BIO6) (°C)
BIO8	Mean temperature of wettest quarter (°C)
BIO9	Mean temperature of driest quarter (°C)
BIO10	Mean temperature of warmest quarter (°C)
BIO11	Mean temperature of coldest quarter (°C)
BIO12	Annual precipitation (mm)
BIO13	Precipitation of wettest month (mm)
BIO14	Precipitation of driest month (mm)
BIO15	Precipitation seasonality (coefficient of variation)
BIO16	Precipitation of wettest quarter (mm)
BIO17	Precipitation of driest quarter (mm)
BIO18	Precipitation of warmest quarter (mm)
BIO19	Precipitation of coldest quarter (mm)
Alt	Altitude from the sea level (m)
Slope	Slope in degrees obtained from altitude (%)
Aspect	Aspect in degrees obtained from altitude (Direction)

Obtaining CL Cases Data and Map Producings
The population data and CL patient numbers of 3 provinces and 39 districts (Adana: 15, Mersin: 10 and Diyarbakir: 14) of the study areas between 2008-2015 were accessed from related institution's databases (TMoH, 2016), (Table 2).

Table 2. Cutaneous Leishmaniasis Cases in Adana, Mersin and Diyarbakir Provinces between 2008-2015

Districts/Years	2008	2009	2010	2011	2012	2013	2014	2015	Total
ADANA	216	330	371	315	179	219	232	118	1980
MERSIN	98	108	70	64	46	38	52	92	568
MEDITERRANEAN	**314**	**438**	**441**	**379**	**225**	**257**	**284**	**210**	**2548**
DIYARBAKIR	93	73	154	86	41	8	22	19	496
TIGRIS	**93**	**73**	**154**	**86**	**41**	**8**	**22**	**19**	**496**
TOTAL	**407**	**511**	**595**	**465**	**266**	**265**	**306**	**229**	**3044**

Ecological Niche Modeling
In the study, we used the distribution of cases as if it was a vector sand fly species for producing ENM of CL (Abdullah et al., 2017). We can identify the distribution of sand flies in an understandable manner with the same environmental variables used to model the distribution of CL. Recently, the maximum entropy model is used for this purpose. Maximum entropy (MaxEnt) models were utilized in this study using the MaxEnt v3.3.3 software. Maxent software is freely downloadable at http://www.cs.princeton.edu/~schapire/maxen.

For the ENM, a file was prepared for proven vector species P. tobbi with several environmental variables in ASCII format and entered into MaxEnt software. Totally 3044 CL cases were included for the modeling construct the remaining 25% data were used in testing the model (Sofizadeh et al., 2017). The software was used with its default parameters with 10,000 as the maximum number of background absences, 0.00001 convergent thresholds, 15 replicates and 5000 as the maximum numbers of iterations and a logistic output presenting a continuous presence probability ranging from 0 to 1. A Jackknife procedure was worked to calculate the contribution of each variable in the modeling process. The area under the curve (AUC) and receiver operating characteristic curve (ROC) was found for the model (Phillips et al., 2006). Also a probability threshold representing the 10th percentile training presence points was selected as a cutoff probability used to convert continuous probability maps for today.

For novel CL model, Maxent software was used that based on a maximum entropy algorithm . The Jackknife test has played an important role in the calculation of the most contributed variables in producing model. In the conducted study, we focused in four contributed variables with the highest percentage, to better understanding of environmental requirements of CL, which were set apart from others. For model prediction in the current, the area under the curve (AUC) which categorized as higher predictive power (AUC > 0.5), random chance (AUC = 0.5) and worse than random (AUC < 0.5), and receiver operating characteristic curve (ROC) was found.

RESULTS AND DISCUSSION

Total 2548 CL patients were reported in 25 districts of two cities in the Eastern Mediterranean Region between 2008 and 2015. Also 496 CL cases reported in Diyarbakir, located in Tigris Basin. Produced model's AUC values were calculated as 0.868, 0.918 (Figure 3) and 0.924 (Figure 4) in Adana Mersin and Diyarbakir, respectively. This means, for the model prediction in the current, the area under the curve (AUC) categorized as higher predictive power (AUC > 0.5) for both three provinces.

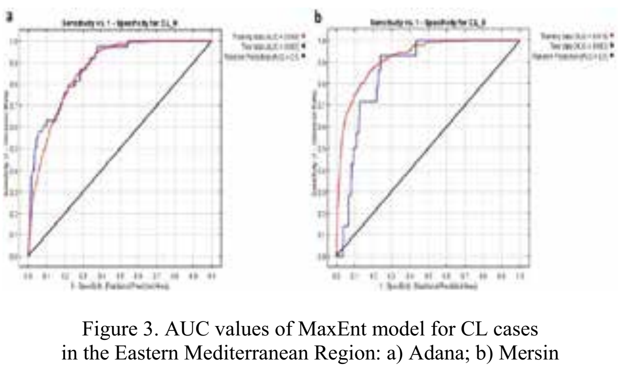

Figure 3. AUC values of MaxEnt model for CL cases in the Eastern Mediterranean Region: a) Adana; b) Mersin

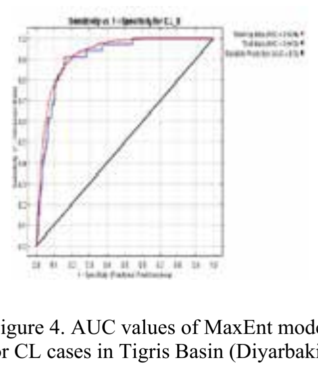

Figure 4. AUC values of MaxEnt model for CL cases in Tigris Basin (Diyarbakir)

Our results included estimation of CL cases possible distribution in the present in two endemic geographical foci, were emphasized in Figures 5 (a, b) and 6. The maps predict that, CL cases epidemiology marked in yellow and red will expanding the central and southeastern parts of Adana (Karaisali, Seyhan and Kozan districts), central and northeastern parts of Mersin (Mut, Silifke and Tarsus districts) in the Eastern Mediterranean Region. Also, Northern parts of Diyarbakir, especially coast of the Tigris river, are more risky in terms of CL than other areas in Tigris Basin.

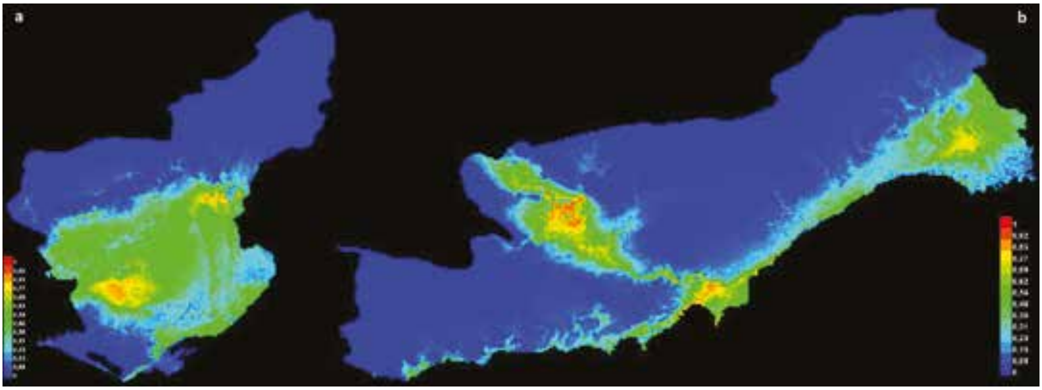

Figure 5. CL cases probable epidemiology in East Mediterranean Region: a) Adana; b) Mersin

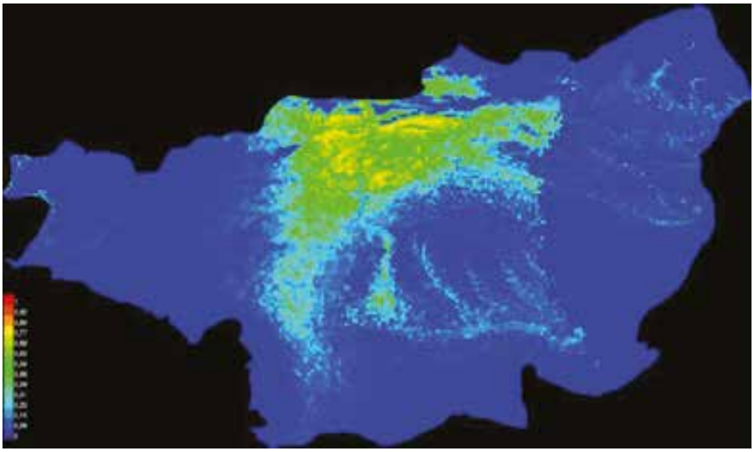

Figure 6. CL cases probable epidemiology in Tigris Basin (Diyarbakir)

In the determination of the most effective factors in the distribution of CL cases in current time, Jackknife analysis was performed with 19 bioclimatic variables and three geographic variables (Table 1). The cross comparison of 22 data groups revealed that, 9 variables were effective with higher contribution to CL distribution.

However, BIO1 (Annual mean temperature), BIO4 (Temperature seasonality) and DEM (Digital elevation model) were significantly associated with the presence of native human CL cases in the current time in Adana. BIO5 (Max temperature of warmest month), BIO9 (Mean temperature of driest quarter) and BIO10 (Mean temperature of warmest quarter) were found more effective factors in CL cases distributionin Mersin. In Diyarbakir, BIO2 (Mean diurnal range), BIO4 and BIO11(Mean temperature of coldest quarter) were detected found to be more effective factors.

In accordance with our MaxENT results, the total accuracy (training gain) of the model in the presence of all variables were approximately 0.92 and 1.42 in Adana and Mersin respectively. Also, it calculated as 1.41 for in Diyarbakir (Figures 7 and 8).

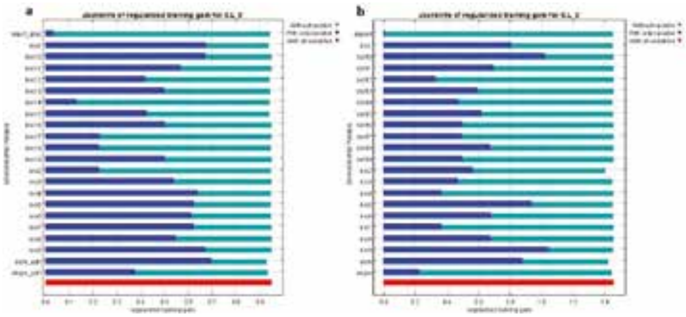

Figure 7. Regularized training gain for CL in East Mediterranean Region: a) Adana; b) Mersin

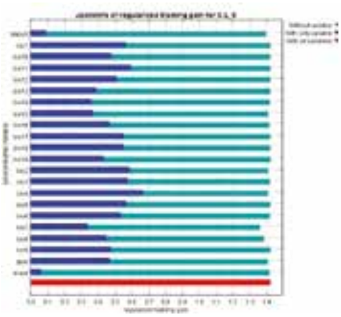

Figure 8. Regularized training gain for CL in Tigris Basin

In evaluation of the most effective bioclimatic and environmental variables in epidemiology of native CL cases in current time for both geographical endemic foci.

In the Eastern Mediterranean Region we observed 5 bioclimatics and one environmental variables were related to neglected diseases called leishmaniasis. In Adana occurrence of CL cases were currently directly related to BIO1, BIO4 was found positive and negative inclined with CL patients probable occurrence and DEM was found inversely related to CL cases distribution (Figure 9.a, Figure 9.b and Figure 9.c). BIO5, BIO9 and BIO10 were found directly related with the CL cases occurrence in Mersin (Figure 9.d, Figure 9.e and Figure 9.f).

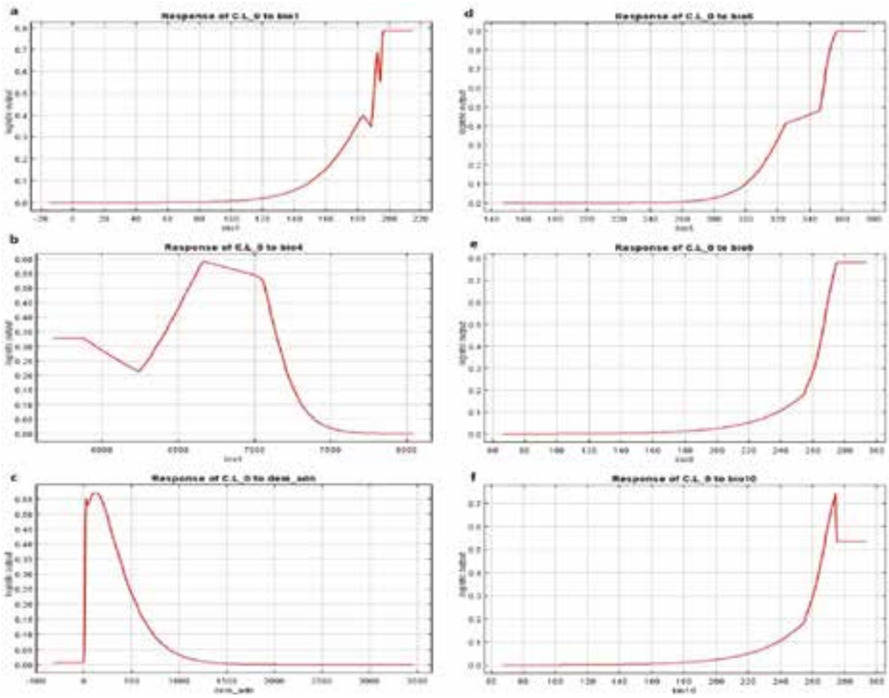

Figure 9. Response of CL cases to significantly associated in East Mediterranean Region: a) Annual mean temperature in current; b) Temperature seasonality in current; c) Digital elevation model in current; d) Max temperature of warmest month; e) Mean temperature of driest quarter; f) Mean temperature of warmest quarter.

In Tigris Basin (Diyarbakir), BIO2, BIO4 and BIO11 were found positive and negative inclined with CL cases distribution (Figure 10).

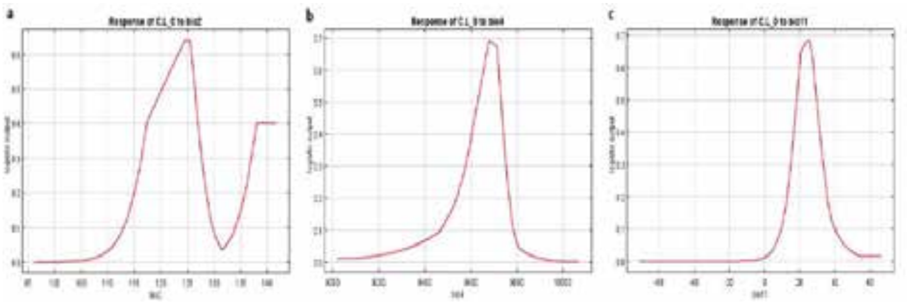

Figure 10. Response of CL cases to significantly associated in Tigris Basin:
a) Mean diurnal range; b) Temperature seasonality; c) Mean temperature of coldest quarter

Especially low socioeconomic level peripheral areas of focused cities, have high number CL patients in two endemic foci of Turkey. Various computer software, included geostatistical tools, used epidemiological prediction of disease in current and future projection.The present MaxENT model helps us to better understanding of comparison of CL current status between two focused endemic foci.

In our study, ecological niche models were compared for two endemic areas and only data from CL patients were used.Although data on the patient and disease agent are theoretically used in risk analyzes, the models produced by MaxENT are preferred, especially in countries where records of CL cases are not accurately reported (Abdullah et al., 2017; Adegboye et al., 2017).

In the present model, it was found that all the three calculated AUC values were above 0.5 and the predictive power was very high (Philips et al., 2006).

When the current model is taken into consideration, it is seen that the Mediterranean Region is more risky than the Tigris Basin in terms of possible increasing in distribution of CL.

When two bio-climatic data were compared for two endemic areas, it was observed that the temperature data of the cold seasons were associated with CL distribution in Tigris Basin. On the contrary, in the Eastern Mediterranean Region where temperate seasons conditions are dominant, it is observed that the bio-climatic data of the hot period is more correlated with CL distribution.

In previous studies, which predict the future distribution of the disease, it is foreseen that the disease will spread to larger areas than the current distribution of the disease, especially in Adana and Diyarbakır (Artun, 2018; Artun & Kavur, 2019).

Totally 3044 CL cases information, reported between 2008 and 2015, were included in this study while 3671 patients were added in a previous study in Bangladesh. In addition AUC value of the Eastern Mediterranean Region were calculated as 0.868, 0.918 and Tigris Basin's AUC was 0.924. These values were close to visceral leishmaniasis prediction (VL) AUC value in Bangladesh, calculated as 0.842. Differently, influential variables were LST (Land use/land cover category), Normalized difference vegetation index (NDVI), Precipitation seasonality, Precipitation of the warmest quarter, Drainage and General soil type (GST) (Abdullah et al., 2017).

In the former study included, the information of the CL patients reported in Iran between 2007-2016, prediction of the possible distribution the vector of the disease and the its reservoir, the AUC values were estimated as high as the AUC value in our model and were calculated as 0.955 and 0.914, respectively, for the two living things (Shiravand et al., 2018).

In conclusion, bioclimatic data are likely to be compatible with each other in the ecological models of the vector sand fly and the disease it infects. The study focusing on CL epidemiology comparison of two endemic foci in Turkey is thought to contribute to the literature as a new study by ENM.

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