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RESEARCH ARTICLE

A New Approach for Determining the Spatial Risk Levels for Visceral and Cutaneous Leishmaniasis related with the Distribution of Vector Species in Western Part of Turkey using Geographical Information Systems and Remote Sensing [1]

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Summary

Leishmaniases are present in two clinical forms, as visceral and cutaneous, in Turkey showing a tendency of spreading throughout the country. The aim of the present study was to produce a new model for determining the spatial risk levels using the data in a selected study site in the western part of Turkey. The results of entomological studies in this leishmaniasis focus indicated the presence of suspected vector species *Phlebotomus (Larroussius) tobbi* and *P. (Larroussius) neglectus* for the visceral, *P. (Paraphlebotomus) similis* for cutaneous forms of the disease. The new risk model was developed based on univariate and multivariate binary logistic regression analyses of geographical variables as altitude, aspect, Normalized Difference Vegetation Index (NDVI), Enhanced Vegetation Index (EVI) and Land Surface Temperature (LST) values related to the distribution of these three species. The results of the new model were used to produce the risk maps and the potential distribution areas of the incriminated vector species with the use of geographical technologies which allowed the identification of the leishmaniasis risk levels that may provide useful information to guide the control program interventions.

Keywords: *Leishmaniasis, Cutaneous, Visceral, Geographical information systems, Risk model*

Coğrafi Bilgi Sistemleri ve Uzaktan Algılama Kullanılarak Türkiye'nin Batısında Visseral ve Kutanöz Leishmaniasisde Vektör Türlerin Dağılımı ile İlişkili Mekansal Risk Düzeylerinin Saptanması Için Yeni Bir Yaklaşım

Özet

Leishmaniasis Türkiye'de visseral ve kutanöz olmak üzere iki klinik formda görülmekte ve bütün ülkeye yayılma eğilimi göstermektedir. Bu çalışmanın amacı, Türkiye'nin batısında seçilmiş bir çalışma alanındaki verileri kullanarak mekansal risk düzeylerini saptamak için yeni bir model geliştirmektir. Bu leishmaniasis odağındaki entomolojik çalışmalarda visseral leishmaniasis için şüpheli vektörler olan *Phlebotomus (Larroussius) neglectus* ve *P. (Larroussius) tobbi,* kutanöz leishmaniasis şüpheli vektör olan *P. (Paraphlebotomus) similis*'in varlığı ortaya konulmuştur. Yeni risk modeli, bu üç türün dağılımları ile ilişkili olarak yükselti, bakı, Normalize Edilmiş Vejetasyon Indeksi (NDVI), Zenginleştirilmiş Vejetasyon Indeksi (EVI), Yüzey sıcaklığı (LST) gibi coğrafi değişkenlerin tek ve çok değişkenli binary logistik regresyon analizlerinden elde edilen değerler esas alınarak geliştirilmiştir. Yeni modelin sonuçları, leishmaniasis risk düzeylerinin tanımlanmasına izin verecek coğrafi teknolojiler kullanarak şüpheli vektör türlerin potansiyel dağılım alanlarını belirleyip risk haritaları üretmek için kullanılmıştır. Bu haritaların da hastalıkla ilişkili kontrol programlarına rehberlik yapacak faydalı bilgiler sağladığı düşünülmektedir.

Anahtar sözcükler: *Leishmaniasis, Kutanöz, Visseral, Coğrafi bilgi sistemleri, Risk modeli*

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INTRODUCTION

Two clinical types of leishmaniasis; zoonotic visceral leishmaniasis (VL) caused by *Leishmania infantum* and anthroponotic cutaneous leishmaniasis (CL) caused by *L. tropica* and *L. infantum* have been reported in Turkey. The zoonotic VL is seen in Aegean, Mediterranean and Central Anatolia Regions endemically and has been found sporadically in other regions. Cutaneous type, which is generally reported from Southeastern (Şanlıurfa province) and the Eastern Mediterranean (Adana, Osmaniye, Mersin, Hatay provinces) parts of Turkey, has been detected in increasing numbers in western part of Turkey related to different risk factors [1].

Aydın province where our study site is located, has important factors as; suitable ecological environment for the maintenance of a vector population and the presence of susceptible human population to *Leishmania* infection. These factors has been reported to assist the emergence of anthroponotic cutaneous leishmaniasis, in the area and a total of 37 and 19 CL patients were diagnosed in 2009 and 2010 in Aydın, respectively (MoH statistics). This region is therefore has been considered as the first region in western Turkey to have indigenous CL cases and a new focus for the disease in Turkey [2,3]. Human and canine visceral leishmaniasis cases have also been reported from Kuşadası, a town belonging to Aydın province, since 1993 [4-6]. In Kuşadası, the seroprevalence of CanL among dogs is found be 16.6%, which is higher than the average ratio of 5.3% (range 3.6% - 25%) in western Turkey [7]. These studies also showed that the one-third of the dogs in an endemic area for CanL could be asymptomatic [5,6].

To date there are twenty-one species of *Phlebotomus* (belonging to the subgenus *Phlebotomus*, *Adlerius*, *Paraphlebotomus*, and *Larroussius*) and four species of *Sergentomyia* known to be present and at least nine species of sand flies have been incriminated as vectors in Turkey [8,9]. Because of the location and geographical diversity causing various climate types and ecological conditions in Turkey, extensive entomological surveys are needed to determine the sand fly fauna, and modeling studies to understand the risks and to develop integrated control measures. In previous studies, *P. neglectus, P. tobbi* are reported as the potential vectors of VL, while *P. similis* is incriminated as the vector of CL in Aydın province [3,8].

Risk models in epidemiology are reported to characterize spatial validation in recent risk of infection and potential causes of that variation. Otsfeld et al.[10] defined ecological risk as the probability of exposure to an infection in the absence of active preventive measures. Risk models for specific diseases are widely based on distribution of vectors, reservoirs and the disease incidence. In this study vector based risk mapping is preferred for the availability to provide sufficient data.

The aim of the present study was to carry out entomological survey and produce a new model for leishmaniases risks using the data related to probable vector species and geographical parameters in a selected study site in the western part of Turkey.

MATERIAL and METHODS

Study Area

The study area is surrounded by southern slopes of The Aydin Mountains from north, Buyuk Menderes Rift Valley from south and Aegean Sea from west which is located in the western part of Turkey *(Fig. 1)*. The Buyuk Menderes Rift Valley is a broad, with flat bottom and steep side, thus creating a natural east-west corridor across West Anatolia. The land use pattern is mostly cotton and corn in valley, vineyards in the slopes. Natural vegetation is mainly maquies in low-land and forests in highlands. The study area has typically Mediterranean climate which is wet in the winter dry in the summer. Mean temperature is 16°C (max 23.2; min 8.1°C), 17.6°C (max 27.3; min 7.8°C) in Kuşadası and Aydın meteorological stations, respectively. Annual mean rainfall is 677.5 mm, over 75% of which precipitation in the wet season from autumn to winter.

The reasons for choosing this area were; **(i)** Kuşadası town has been known as endemic area for human and canine visceral leishmaniasis caused by *L. infantum* MON1 and MON98 for long time, and **(ii)** Aydın province has been known as endemic area for anthroponotic cutaneous leishmaniasis caused by *L. tropica* MON303 and canine leishmaniasis has recently been determined in the area. The study area was 48x88 km^2 and it was divided 66 squares as 16 km^2 each. The field work has been carried in two periods; between 8 and 15 July 2006, and between 6 and 13 July 2007.

Sand Fly Collection

The chosen study area was 48x88 km^2 and divided to 66 squares as 16 km^2 each and at least one location was selected in each square, and a total of 132 localities were chosen during the work. Sand fly collection was done in the summer season of 2006 and 2007. In each locality, 5-20 sticky paper traps (A4 size) were placed into the holes on the embankment walls. A total of 1119 sticky paper traps were set up and left for four days. At the end of the period, 997 (89.09%) of them were recovered. Detailed information about environment and trapping in the each location was collected using Pendragon software in palm PC. These data were transferred to the PC and stored at an excel file.

Data Sources and Analyses

The data sets were obtained in two categories: **(1)** environmental data corresponding to the coordinates of

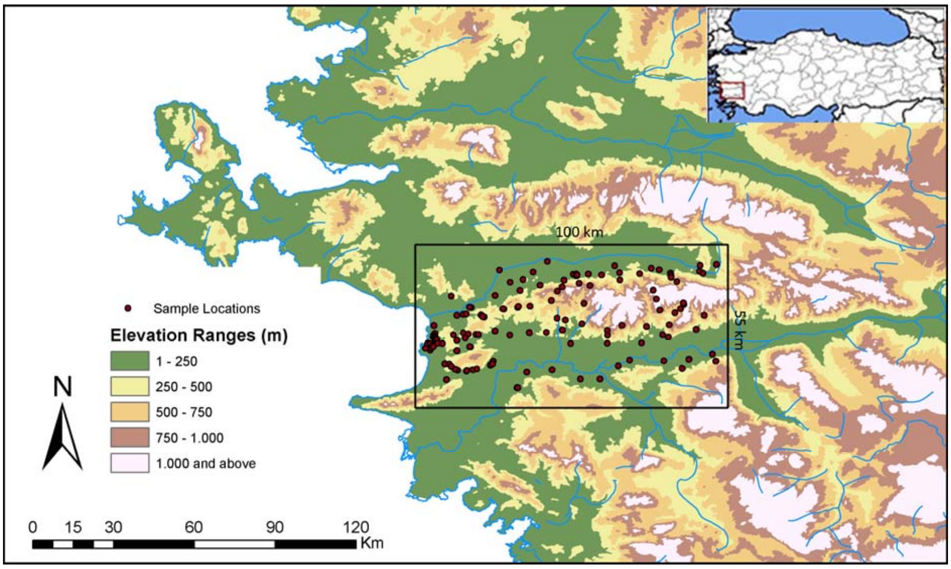

Fig 1. The distribution of the locations in the study area

Şekil 1. Çalışma alanında lokalitelerin dağılımı

each location of sand fly samples were extracted from topographical and remotely sensed images. Data on elevation, slope and aspect of the study area were derived from 3 arc second resolution SRTM (Shuttle Radar Topography Mission worldwide elevation data), NDVI, EVI and LST were obtained from Landsat ETM + (path 180, row 34) and MODIS data set. For MODIS data, temperature and reflectance layers were extracted from MOD11A2 and MOD43B4 files (The MOD11A2 product contains an 8-day average of land surface temperature at 1-kilometre resolution. MOD43B4 imagery comprises 16-day composites of reflectance for seven wavelength bands, also at 1-km resolution) for the years 2001 through 2005. Reflectance bands were combined to create two vegetation indices, NDVI and EVI. A set of nine measures, or channels, was then processed by a temporal Fourier algorithm: middle infra-red reflectance, daytime land surface temperature, night time land surface temperature, NDVI, EVI, evapotranspiration, latent heat flux/transfer, potential evapotranspiration, and potential latent heat flux/transfer.

Model Validation

The ACL patient's records between the years of 2002 and 2009 were obtained from Ministry of Health (MoH). These patients' information was used for the validation of the produced risk maps. Data mentioning the nearest settlement of 113 CL patients were geo-positioned using GIS tools.

Statistical Analysis

All statistical analysis was done using SPSS v.15 statistical package. An univariate binary logistic regression analysis was initially undertaken to determine the relationship between three vector species (*P. neglectus, P. tobbi, P. similis*) and several geographical variables. Stepwise multivariate analysis was then carried out by binary logistic regression to determine predictor variables affecting presence of ACL, respectively. For the logistic model, all 132 locations were used in the analysis. The results were recorded in the GIS software to create risk model and then maps.

RESULTS

In the study period, a total of 721 sand flies were collected and 276 and 445 of them were belonging to *Phlebotomus* and *Sergentomyia* genera, respectively. The densities of vector species were analyzed together according to the altitudinal range. *P. neglectus* is present in each altitudes but it has only three peaks in 100-200; 300-400 and 800-900 meters. *P. tobbi* is not present in each altitude, but it has only two peaks in 200-300 and 300-400 meters. *P. similis* is present in each altitude till 800 meters and it has two peaks in 0-100 and 700-800 meters *(Fig. 2)*.

The results of the univariate analysis of the relationship of ACL presence with different environmental variables are shown in *Table 1*. The probability of presence of vector species in a particular location appeared to be significantly correlated with the day and night time LST values, NDVI or EVI values and DEM *(Table 1)*. Multivariate analysis results are presented in *Table 2*. The presences of three vector species were individually associated with one or more parameters as: daytime LST (maximum and phase of biannual cycle), NDVI (maximum and variance of biannual cycle) and EVI (mean & phase of biannual cycle).

Proposed Risk Model

Weighted score analysis is used to create the risk model. The weighted score was calculated for every significant ($P<0.005$) environmental variable (Ev) derived from univariate logistic regression analysis.

$$W_i = (1 - p_i)$$

Weighted scores (w_i) were used to determine Risk

***Table 1.** Correlation of presence of vector sand fly species with different environmental variables (univariate binary logistic regression analysis) *** highly significant (< 0.001); ** very significant (<0.002); * significant (<0.05)*

***Tablo 1.** Farklı çevresel değişkenler ile vektör kum sineği türlerinin varlığının korelasyonu (tek değişkenli binary lojistik regresyon analizi) *** yüksek derecede anlamlı (< 0.001); ** çok anlamlı (<0.002); anlamlı (<0.05)*

Variables	P-values		
	P. neglectus	***P. tobbi***	***P. similis***
Day-time Land Surface Temperature			
Daytime LST amplitude of annual cycle	0.112	0.062	0.008*
Daytime LST amplitude of biannual cycle	0.175	0.452	0.000***
Daytime LST amplitude of triannual cycle	0.328	0.008*	0.630
Daytime LST minimum	0.001***	0.647	0.002**
Daytime LST maximum	0.639	0.032*	0.062
Daytime LST phase of biannual cycle	0.479	0.040*	0.578
Daytime LST phase of triannual cycle	0.136	0.034*	0.324
Night-time Land Surface Temperature			
Night-time mean LST	0.006*	0.490	0.008*
Night-time LST amplitude of annual cycle	0.600	0.992	0.025*
Night-time LST variance in triannual cycle	0.049*	0.795	0.076
Night-time LST minimum	0.020*	0.540	0.002**
Night-time LST maximum	0.015*	0.372	0.133
Normalized Difference Vegetation Index			
Mean NDVI	0.000***	0.009*	0.006*
NDVI amplitude of annual cycle	0.109	0.019*	0.910
NDVI amplitude of triannual cycle	0.869	0.010*	0.454
NDVI minimum	0.001***	0.135	0.005*
NDVI maximum	0.000***	0.001***	0.032*
NDVI phase of biannual cycle	0.001***	0.933	0.003*
Enhanced Vegetation Index			
Mean EVI	0.000***	0.000***	0.001***
EVI amplitude of annual cycle	0.016*	0.234	0.262
EVI variance in annual cycle	0.026*	0.236	0.215
EVI variance in triannual cycle	0.043*	0.191	0.027*
EVI mimimum	0.003*	0.013*	0.004*
EVI maximum	00.001***	0.007*	0.024*
EVI phase of biannual cycle	0.003*	0.416	0.002**
Non-MODIS Variables			
DEM (SRTM)	0.000***	0.369	0.002**
NDVI (LANDSAT)	0.010*	0.177	0.193

values (Rv). Risk value for each species is independently modeled as follows;

$$Rv = 1/\log(w_1Ev_1+w_2Ev_2+\dots\dots\dots+w_nEv_n)$$

Risk value maps related to three probable vector species (*P. similis, P. tobbi* and *P. neglectus*) were created based on MODIS, Landsat and SRTM data sets (*Fig. 3* and *4*).

The risk levels for space produced from the model were categorized as 10 -high to 1-low.

Validation

For validation of the Cutaneous Leishmaniasis Risk Map, the settlement coordinates of the previously proven CL patients were overlaid on the risk map. The risk levels were grouped as high, moderate and low, while the validation of the model was tested based on number of cases in each risk levels *(Table 3, Fig. 5)*.

DISCUSSION

Recent developments in geographical technologies (GIS, remote sensing, GPS) have given invaluable tools to researchers for analyzing the vector borne diseases such as malaria, leishmaniases and related environmental factors affecting their spatio-temporal distribution [11].

Disease risk or incidence is found to be more closely correlated with the abundance of pathogen-infected/infective vectors, rather than with the presence or total abundance of vectors and the direct causal relationship linking environmental conditions to vector distribution or abundance remains to be established. There are different ways for using of maps in epidemiology of an arthropod-borne disease and particular arthropod vector, vertebrate reservoirs and cases of disease in humans (or incidence) represent distinct challenges for the mapping of the disease risk. In our study, we produced the maps related to particular arthropod vector species presence and absence but we have to take into account the limitations of vector based risk mapping as they have been described earlier. First, disease risk or incidence is more closely correlated with the abundance of pathogen-infected vectors, rather than with simply presence of vectors, or total abundance of vectors [10].

Table 2. *Correlation of presence of vector sand fly species with different environmental variables (multivariate binary logistic regression analysis)*

Tablo 2. *Farklı çevresel değişkenler ile vektör kum sineği türlerinin varlığının korelasyonu (çok değişkenli binary lojistik regresyon analizi)*

Variables	P-values		
	P. neglectus	*P. tobbi*	*P. similis*
Land Surface Temperature			
Daytime LST maximum	-	-	0.001
Daytime LST phase of biannual cycle	-	0.001	-
Normalized Difference Vegetation Index			
NDVI maximum	0.0014	-	-
NDVI variance in annual cycle	-	0.003	-
Enhanced Vegetation Index			
Mean EVI	-	0.000	-
EVI phase of biannual cycle	-	-	0.000

Table 3. *The frequency of cutaneous leishmaniasis cases in different risk levels*

Tablo 3. *Farklı risk düzeylerinde kutanöz leishmaniasis olgularının sıklığı*

Risk Levels for Space	No of CL cases	%
High	57	50.45
Moderate	29	25.66
Low	27	23.89
Total	113	100

All vector borne diseases have been influenced by environmental factors, distribution of vector species and their population sizes, possible reservoirs in the endemic areas and human activities. Understanding the relation between leishmaniasis and environmental variables is important for planning and implementation of integrated control strategies for vector borne diseases. Although, especially in the recent years, the studies focused on determining risk levels of leishmaniases are getting increased, they are mostly based on multivariate logistic regression prediction models [12-16]. There are no studies on this issue in Turkey. The present study investigates the risk levels of producing a predictive risk map of human visceral and cutaneous leishmaniases for western Turkey, based on the database obtaining during EU-EDEN Project (Emerging Diseases in a Changing European Environment; http://www.eden-fp6project.net). The model described in the current study is developed with the modification of multivariate logistic regression prediction models. The produced risk maps would allow health policy makers for control programs to identify the problem in the different areas and use intervention reasonably.

The data related with environmental variables and

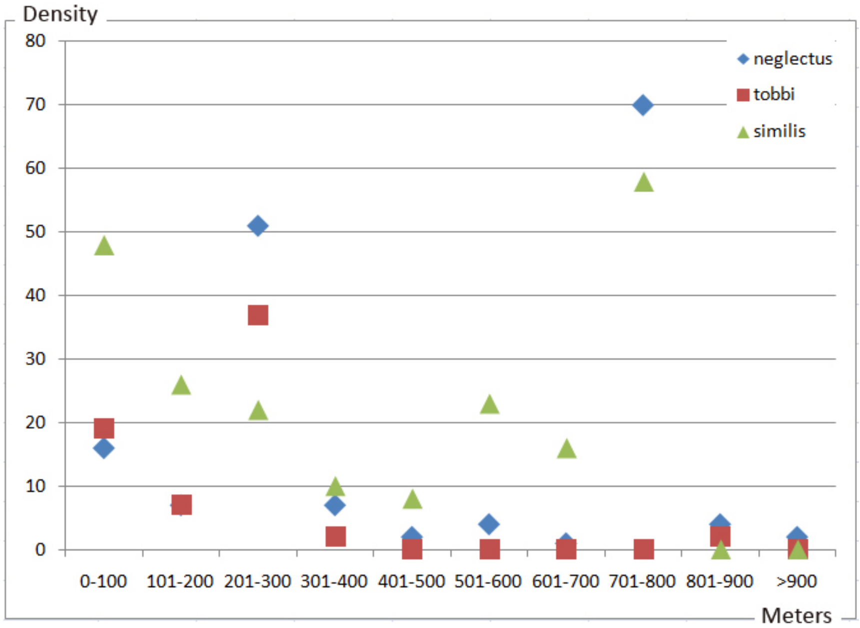

Fig 2. The density of vector sand fly species according to the altitude in the study area

Şekil 2. Çalışma alanında vektör kum sineği türlerinin yükseltiye göre bulunma sıklıkları

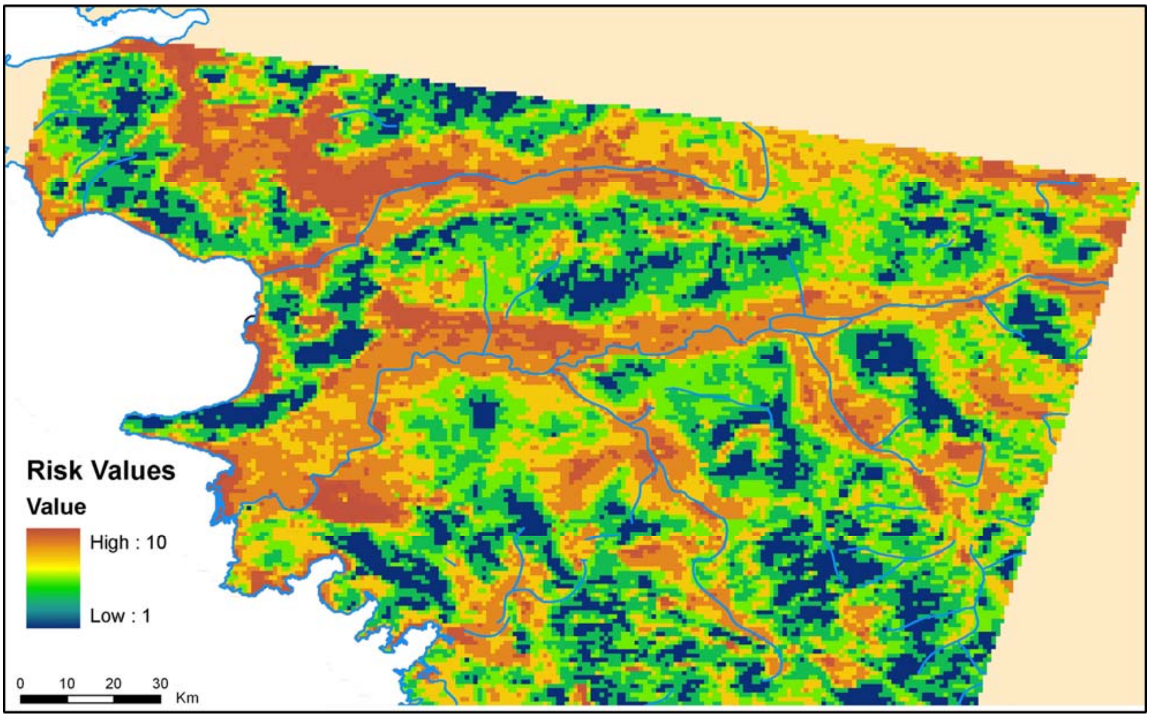

Fig 3. Risk Value map for cutaneous leishmaniasis based on data sets related to *P. similis*

Şekil 3. *P. similis* ile ilişkili verilerden yola çıkılarak hazırlanan kutanöz leishmaniasis risk haritası

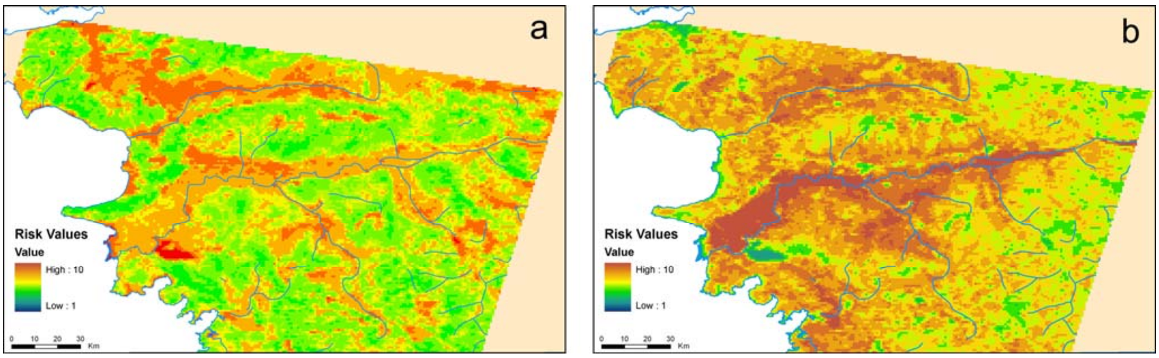

Fig 4. Risk Value maps for visceral leishmaniasis based on data sets related to (a) *P. neglectus* (b) *P. tobbi*

Şekil 4. (a) *P. neglectus* ve (b) *P. tobbi* ile ilişkili verilerden yola çıkılarak hazırlanan visseral leishmaniasis risk haritası

sand fly collection used for creating the new model was obtained during the above mentioned project. The official records about local ACL patients were gathered from the local Branch of the MoH and georeferenced accordingly. Therefore, patients apply to health centers when they suspect the disease and this makes it a very reliable patient data.

Firstly, identified different number of values of significance related with three vector species in each group of variables (Day Time LST, Night Time LST, NDVI, EVI and DEM) was taken into consideration as a result of univariate logistic regression analysis *(Table 1)*. Secondly, the only significant variables (P>0.05) were included in the multivariate logistic regression analysis showed that the significance values of NDVI maximum for *P. neglectus*, Daytime LST phase of biannual cycle, NDVI variance in annual cycle and Mean EVI for *P. tobbi* and Mean EVI for *P. similis*. The values that are generated from multivariate analysis were applied to the determining the weighted score for each significant environmental variable, then the weighted scores applied to the Risk Value (Rv) equation. The presence of all three species was associated with population size and vegetation, only *P. tobbi* and *P. similis* have been associated with land surface temperature.

Eleven different *Phlebotomus* species were found in the study area including vector species, *P. tobbi, P. neglectus* & *P. similis*. The vector species had equal distribution in the west and east sectors of the area. Altitude is found to be related to the density of sand flies *(Fig. 2)*. Site location and aspect of the wall were found as useful indicators for predicting the density of *P. tobbi* and *P. neglectus* (data not shown).

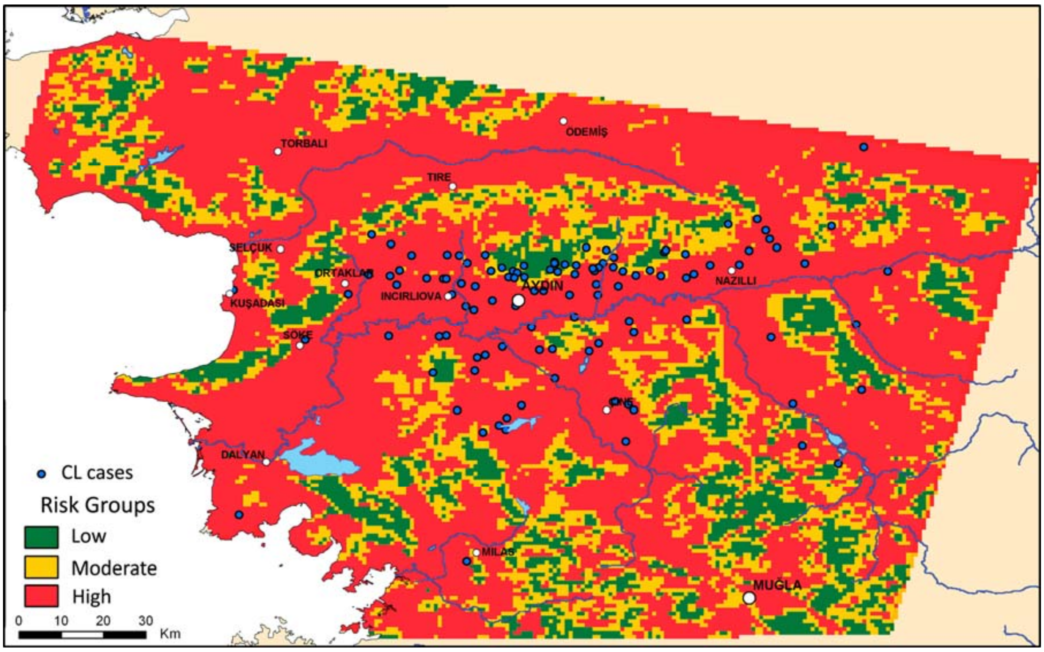

Fig 5. The validation of the cutaneous leishmaniasis risk map with the data of cutaneous leishmaniasis cases from the study area

Şekil 5. Çalışma alanındaki kutanöz leishmanaisis olgularına ait veriler ile kutanöz leishmaniasis risk haritasının onaylanması

In the study area, *P. neglectus,* which is considered as the probable vector species for zoonotic VL and CanL, is present in every altitude range with different densities and in the locations where CanL has reported to have a high seroprevalence rate in all study area [5,7]. *P. tobbi* is only present between 200 and 400 meter above sea level and no actual relation was found with previously reported CanL cases in the study area. *P. similis*, the probable vector species of ACL, was found to be present in the altitudes between 100-900 m.

Risk maps with respect to each vector sand fly species distribution in the area is developed using data sets derived from environmental variables obtained from remotely sensed images. The risks maps indicated the probability for the presence of vector species in whole area, increasing in alluvial plains, and decreasing in altitudes higher than 800 m. Risk maps indicated that, spatial probability of the presence of *P. tobbi* is higher than other species.

A correlation was determined between locations of CL cases and presence of *P. similis* on the risk map created. The high number of CL cases in places with a high and moderate risk levels (76.11%), observed in the present study, supports that hypothesis. Validation of VL risk maps could not be performed due to a very low number of VL cases reported from the area. A wide serological survey is needed for the better understanding the seroprevalence of the visceral form of the disease among human and dogs in this particular region.

Although this new approach can be used for other regions of the country to predict and map leishmaniases, each region must be evaluated separately due to its diverse geographical conditions and the presence of different species of the vector *Phlebotomus*.

As a conclusion, the model gave us an important chance to produce risk maps of a particular disease and predict the risk in the areas where preliminary data has not been available. The model may also be applied for other endemic regions for leishmaniasis in Turkey as well as other countries.

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