



Climate change and distribution of zoonotic cutaneous leishmaniasis (ZCL) reservoir and vector species in central Iran

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Abstract

Aim of the study was to investigate the effects of climate change on the potential distribution of the zoonotic cutaneous leishmaniasis (ZCL) reservoir and vector to 2050s in central Iran. The bioclimatic variables (BVs) were obtained from the World Clim global climate data at a resolution of 30 s. MaxEnt software was used for the model predictions by all variables. According to the Representative Concentration Pathway 4.5 (RCP 4.5) Scenario, the area under the curve (AUC) for *Rhombomys opimus* and *Phlebotomus papatasi* was calculated as 0.877 and 0.921, respectively. Jackknife test indicated that BV2 (76.7%) and BV8 (38.1%) had the highest effect on the models for the reservoir and vector, respectively. In the RCP 8.5 scenario, AUC value for *R. opimus* and *P. papatasi* were obtained as 0.851 and 0.913, respectively. Jackknife test displayed that BV7 (73.5%) and BV8 (34.6%) were the most important variables on the model for the reservoir and vector, respectively. Future projections of models indicated that to the 2050s, the climatically suitable area for *P. papatasi* would expand mainly in the western area of the Yazd province, whereas would decrease in the eastern areas. Currently, the presence probability of this species in Bafq city was reported by about 70%. It is projected that in the 2050s, many areas of the province would have a dramatic decline in ZCL distribution. The results of this study will help the health authorities to forecast possible future ZCL transmission dynamics in different areas of Yazd province and to make appropriate decisions in the high-risk areas.

Keywords Climate change · Zoonotic cutaneous leishmaniasis · MaxEnt model · Yazd province

Introduction

The reason for the incidence of cutaneous leishmaniasis (CL) is a protozoan of the genus *Leishmania*. Zoonotic cutaneous leishmaniasis (ZCL) and anthroponotic cutaneous leishmaniasis (ACL) are forms of the disease that is prevalent in Iran (Shirzadi et al. 2015). Vector-borne diseases such as ZCL are usually sensitive to climatic conditions (Mollalo et al. 2015). Recent studies prove that climate change is one of the important factors involved in the increase in the number of cases and the range of ZCL distribution (Tlamcani and Er-Rami 2014). Climatic change can act as a limiting or exacerbating factor in favorable conditions for ZCL which may explain their role in the incidence of the disease. Climate by facilitating the development of the parasite or the synergistic changes in populations of reservoir and vector causes an increase in the vector population and ultimately increases the transmission of the disease (Boussaa et al. 2016). Rainfall can, with increasing the growth of the vegetation, provide suitable breeding places and an increased number of sand fly vectors (Yates et al. 2002). Even minor climate changes can

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affect the distribution of ZCL reservoirs and vectors, density, activity and breeding period (Toumi et al. 2012). Moreover, Climate variability may affect the changes in the vector geographical spreading. It has been found that the population of rodent reservoirs are also extremely sensitive to the accessibility of food in the environment (Nikonahad et al. 2017; Talmoudi et al. 2017). A previous research conducted in Iran identified environmental changes as a major risk factor for the prevalence of ZCL (Mollalo et al. 2015; Shirzadi et al. 2015). The number of days with temperature over 30 °C was correlated to CL incidence. The study conducted in Dehloran, Iran showed that the number of days with temperature over 30 °C was correlated to CL incidence (Nikonahad et al. 2017). Another study also indicated that higher air temperature causes a significant increase in the population of infected sandflies (Trájer et al. 2013). The results of research in Ilam, Iran showed that there was a statistically significant relationship between CL prevalence and environmental variables such as elevation, rainfall, temperature, urban land use, poorland, dry farming, and forest and irrigated lands (Mokhtari et al. 2016). Yazd province due to specific weather conditions is considered one of the main foci of ZCL in central Iran (Shiravand et al. 2018). The prevalence of ZCL was reported in most areas of the world, especially in developing countries. CL is endemic in 88 countries and 90% of cases have been reported from Afghanistan, Pakistan, Saudi Arabia, Turkey, Iran, Syria, Algeria, Brazil and Peru (Postigo 2010; Carnaúba et al. 2009). The prevalence of this species in different areas of Iran has been reported between 1.8 and 37.9% (Nikonahad et al. 2017). Between all of *Leishmania* species, most cases of ZCL outbreak in Yazd province related to *Leishmania major*. This species is isolated from various rodent reservoirs such as *Rhombomys opimus*, *Meriones libycus*, *Tatera indica* and *Meriones persicus* and the sand fly vector *Phlebotomus papatasi*. (Jafari et al. 2013; Yaghoobi-Ershadi et al. 2015).

Representative concentration pathway (RCP) scenarios are a collection of concentration and emission pathways of greenhouse gas designed for survey and assistance of research on climate change effects and potential policy-makers' response to these changes (Van Vuuren et al. 2014; O'Neill et al. 2014). RCP scenarios provide interpolated climate layers based on the 2003 3rd assessment report of the intergovernmental panel on climate change (Shrestha et al. 2016). These scenarios can assume various climate futures according to greenhouse gas emission pathways by 2100 (Shrestha et al. 2016). Overall, a set of four RCPs have been created and are named based on the variation of radiative powering by the end of the century: 8.5, 6, 4.5 and 2.6 W/m². Ecological niche models (ENMs) by the combination of the point's incidence data, environmental layers and other algorithms on a geographic information system (GIS), can provide a good understanding of the distribution

of vector-borne disease for the people, officials, and policy-makers of the study area (Abdullah et al. 2017). Carvalho et al. 2017). ENMs try to forecast the fundamental niche of a species defined as the complex of environmental condition in which it can protect the population without the need for emigration (Alvarado-Serrano and Knowles 2014). The fundamental niche provides the potential distributional pattern of a species when predicted to a geographical space (Soberón 2007). Actually, ENMs combine the ecological and spatial needs of species and predict the incidence of species in a region among the potential and actual distributions (González et al. 2010). So, ENMs can provide a good framework for testing suppositions concerning the role of various environmental variables in determining species' distributional patterns (Sarkar et al. 2006). Estimating the potential future distributions of vector and reservoir ZCL can help to specify potential risk areas of this species. The present study aims to model and predict suitable ecological niches as well as the distribution of the main vector and reservoir species of ZCL in Yazd province.

Materials and methods

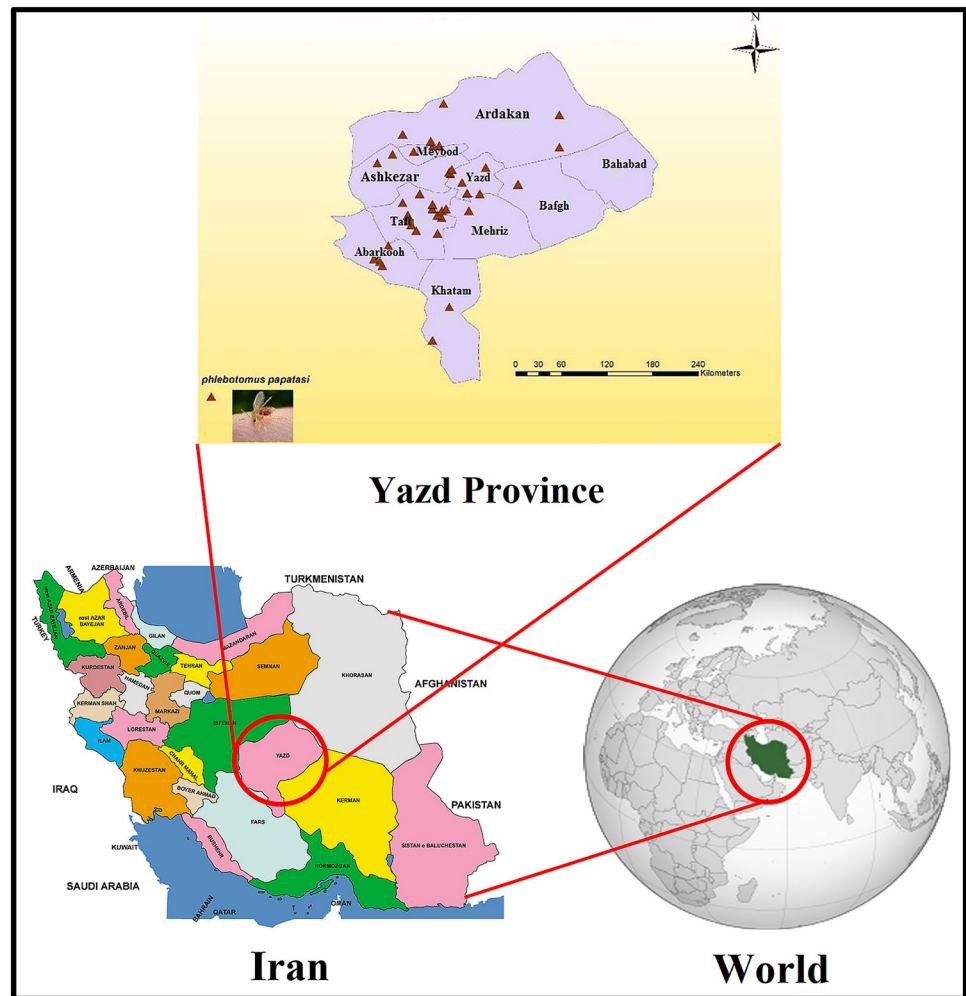
Study area and vector and reservoir data

Yazd province, with a population of about 1.5 million people and with an area of 74,650 km², is situated in the central part of Iran (33_270 N, 56_37 E) (Fig. 1). This province, with a mean annual precipitation of 83 mm and with temperatures above 40 °C in the summer season, is one of the warmest areas in the central desert of Iran (Hajizadeh et al. 2019; Mokhtari et al. 2019). Distribution data for the vector (*P. papatasi*) and reservoir (*R. opimus*) of ZCL in Yazd province were gathered from previous studies conducted between 1989 and 2014. According to information from the provincial health center, we found 38 collection sites for *P. papatasi* and 13 sites for *R. opimus*. Coordinates of the collection sites for these species were also recorded in a database.

General circulation models (GCM)

The results of the research conducted by National Climate Research Institute were the basis for selecting GCM in this study (Ghahreman et al. 2015). The General Circulation Model ACCESS1-0 was used in our analysis at a spatial resolution of 30 s (1 km²). The model output of ACCESS1-0 was prepared for Coupled Model Inter comparison Project phase 5 (CMIP5) of the historical experiment, ensemble r2i1p1. This model was developed as collaboration between BoM and CSIRO. The simulation-based model was a contribution of the Australian Community Climate and Earth System Simulator Coupled Model (ACCESS-CM) to CMIP5

Fig. 1 Distribution of *Phlebotomus papatasi* in Yazd Province in central Iran



(Collier and Uhe 2012). The ACCESS-CM comes in two versions: ACCESS1.0 and ACCESS1.3. The following components are incorporated into ACCESS1.0 model: the UK Met Office UM atmosphere model, the GFDL MOM4p1 ocean model, the LANL CICE4.1 sea-ice model and the MOSES2 land surface model (Collier and Uhe 2012; Lorant et al. 2014). In the present study, two scenarios were used for modeling: RCP4.5 and RCP8.5. In the RCP4.5 scenario, CO₂ concentration is assessed to be 650 PPM by 2100, with a radiative forcing level of 4.5 W/m² (He and Zhou 2015). The Global Change Assessment Model (GCAM) modeling team at the Joint Global Change Research Institute (JGCRI) in the United States developed the RCP 4.5 scenario (Anderson et al. 2016). The RCP 4.5 scenario is considered as a stabilization scenario, without an overshoot, in which total radiative forcing is stabilized shortly after 2100 (Lee et al. 2014). RCP 8.5 scenario corresponds to the maximum greenhouse gas emission trajectory compared to the overall emissions scenario literature (O'Neill et al. 2014), and hence also to the upper bound of the RCPs. In the RCP 8.5 scenario, the greenhouse gas concentrations

and emission trajectories increase considerably over time, leading to a radiative forcing level of 8.5 W/m² at the end of the century with a temperature range between 3.5 and 4.5 °C (Fann et al. 2015). The bioclimatic variable (BV) climatic data based on RCP 4.5 and RCP 8.5 scenarios for the year 2050 were downloaded from www.worldclim.org (http://www.worldclim.org/cmip5_30s).

Bioclimatic, climatic and environmental variables

The bioclimatic and climatic variables were obtained from the WorldClim global climate data at a spatial resolution of the 30s (<http://www.worldclim.org/current>). The environmental variables such as altitude (m), slope (degree) and aspect (direction of slope) were obtained from the Digital Elevation Model (DEM) of Iran using ArcGIS 10.3 at a similar resolution. The layers were converted to ASCII raster by Arc Map for analysis in the MaxEnt model. MaxEnt model was used for prediction by incorporating the variables' temperature, precipitation, altitude, slope, and aspect (Table 1).

Table 1 Variables used to predict the potential distribution of *P. papatasi* and *R. opimus* as vector and reservoir of ZCL in Yazd Province, Central Iran, Horizon 2050, RCP 4.5 and 8.5 scenario and ACCESS1-0 Model

Variable	Description	<i>P. papatasi</i>				<i>R. opimus</i>			
		Contribution (%)		Permutation importance		Contribution (%)		Permutation importance	
		RCP		RCP		RCP		RCP	
		4.5	8.5	4.5	8.5	4.5	8.5	4.5	8.5
Bioclimatic variable 1	Annual mean temperature (°C)	0	0	0	0	0	0	0	0
Bioclimatic variable 2	Mean diurnal range [mean of monthly (max temp–min temp)] (°C)	5.7	1.3	14	0.5	76.7	21.5	60.2	28.6
Bioclimatic variable 3	Isothermality (bioclimatic variable 2/bioclimatic variable 7) (×100)	7.9	15.7	23.8	23.1	0	0	0	0
Bioclimatic variable 4	Temperature seasonality (standard deviation × 100)	7.4	3.1	3.9	4.2	16.7	0	38.3	0
Bioclimatic variable 5	Max temperature of warmest month (°C)	0	0	0	0	0	0	0	0
Bioclimatic variable 6	Min temperature of coldest month (°C)	1.2	0	1.4	0	4	0	0	0
Bioclimatic variable 7	Temperature annual range (bioclimatic variable 5–bioclimatic variable 6) (°C)	8	0	0	0	0	73.5	0	67.6
Bioclimatic variable 8	Mean temperature of wettest quarter (°C)	38.1	34.6	8	0	0	0	0	0
Bioclimatic variable 9	Mean temperature of driest quarter (°C)	0.3	7.9	0.3	29	0	0	0	0
Bioclimatic variable 10	Mean temperature of warmest quarter (°C)	0	0	0	0	0	0	0	0
Bioclimatic variable 11	Mean temperature of coldest quarter (°C)	0	0.4	0	11.6	0	0	0	0
Bioclimatic variable 12	Annual precipitation (mm)	0	2.3	0	6.9	0	0	0	0
Bioclimatic variable 13	Precipitation of wettest month (mm)	7.1	1	28.6	8.8	0	0	0	0
Bioclimatic variable 14	Precipitation of driest month (mm)	0.9	0.5	0	0	0.1	0	0	0
Bioclimatic variable 15	Precipitation seasonality (coefficient of variation)	1.6	12.1	0.9	1.5	0	3.2	0	1.7
Bioclimatic variable 16	Precipitation of wettest quarter (mm)	0	4.7	0	3.4	0	0	0	0
Bioclimatic variable 17	Precipitation of driest quarter (mm)	4.8	0.7	5.3	1.8	0	0	0	0
Bioclimatic variable 18	Precipitation of warmest quarter (mm)	0	4.9	0	0	0	0	0	0
Bioclimatic variable 19	Precipitation of coldest quarter (mm)	0	0.4	0	0	0	0	0	0
Slope	Slope in degrees obtained from altitude (%)	15.7	8.8	12.9	8.5	2.5	1.7	1.5	2.1
Altitude	Altitude from the sea level (m)	0	0	0	0	0	0	0	0
Aspect	Direction of slope (degree)	1.4	1.5	0.8	0.7	0	0	0	0

Modeling potential occurrence of reservoir and vector

MaxEnt software Ver. 3.3.3 was applied to forecast the most proper ecological niches for the target species (Radosavljevic and Anderson 2014). For assessing the contribution of all variables the Jackknife test was used and variables with no contribution were removed from the final test. 80% of the reservoir/vector collection points were used for model training and the remaining 20% were used testing the model. For random point selection MaxEnt model was used.

Results

Modeling for ZCL vector and reservoir, horizon 2050, RCP 4.5 scenario, ACCESS1-0 model

Table 1 displays estimates of relative contributions of the environmental variables to the MaxEnt model for the vector and reservoir of ZCL. According to this table in the RCP 4.5 scenario, the variables that the highest contribution for *P. papatasi* and *R. opimus* were BVs 2 and 8 with a share of 76.7 and 38.1%, respectively. The area under the curve

(AUC) for *P. papatasi* was 0.921. The results of the jackknife test (variable importance) for *P. papatasi* revealed that BV 7 as the environmental variable has the maximum gain when used in isolation. Therefore it appears this variable has alone the most useful information. The environmental variable that reduced the most gain when eliminated from the model was the slope. So, appears slope has more information than the other variables (Fig. 2). The AUC for *R. opimus* was 0.877. So that according to the Jackknife test for *R. opimus*, the BV 2 as an environmental variable when used in isolation, has the highest gain which therefore seems to have the most useful information. Also, the BV 2 was variable that decreased the most gain when omitted from the model. Therefore, seems, unlike the other variables this variable has the most useful information (Fig. 3).

Modeling for ZCL vector and reservoir, horizon 2050, RCP 8.5 scenario, ACCESS1-0 model

Table 1 related to the assessment of the relative contribution of the environmental variables in the MaxEnt model for the vector and reservoir of ZCL. According to this table in the RCP 8.5 scenario, the variables that the highest contribution for *P. papatasi* and *R. opimus* were BVs 7 and 8 with a share of 73.5 and 34.6%, respectively. The AUC for *P. papatasi* was 0.913. So that according to the results of the Jackknife test for *P. papatasi*, BV 8 as the environmental variable has the maximum gain, when used in isolation. Therefore seems that BV 8 has the most useful information by itself. The BV 3 was an environmental variable that decreased the most gain when omitted from the model. Therefore, seems unlike the

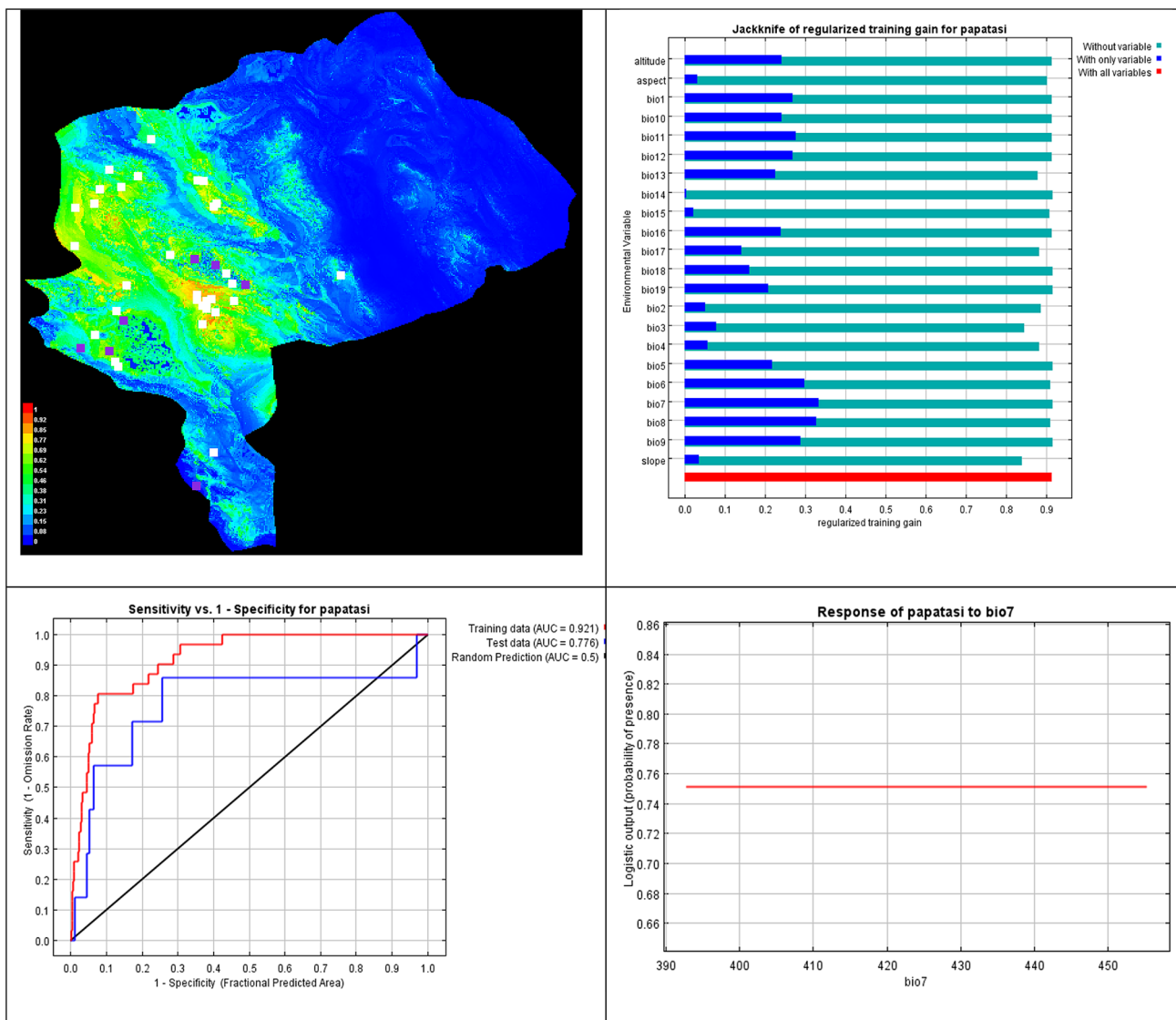


Fig. 2 Result of Maxent model and jackknife test for *P. papatasi* in province of Yazd, Horizon 2050, RCP 4.5 scenario, and ACCESS1-0 Model

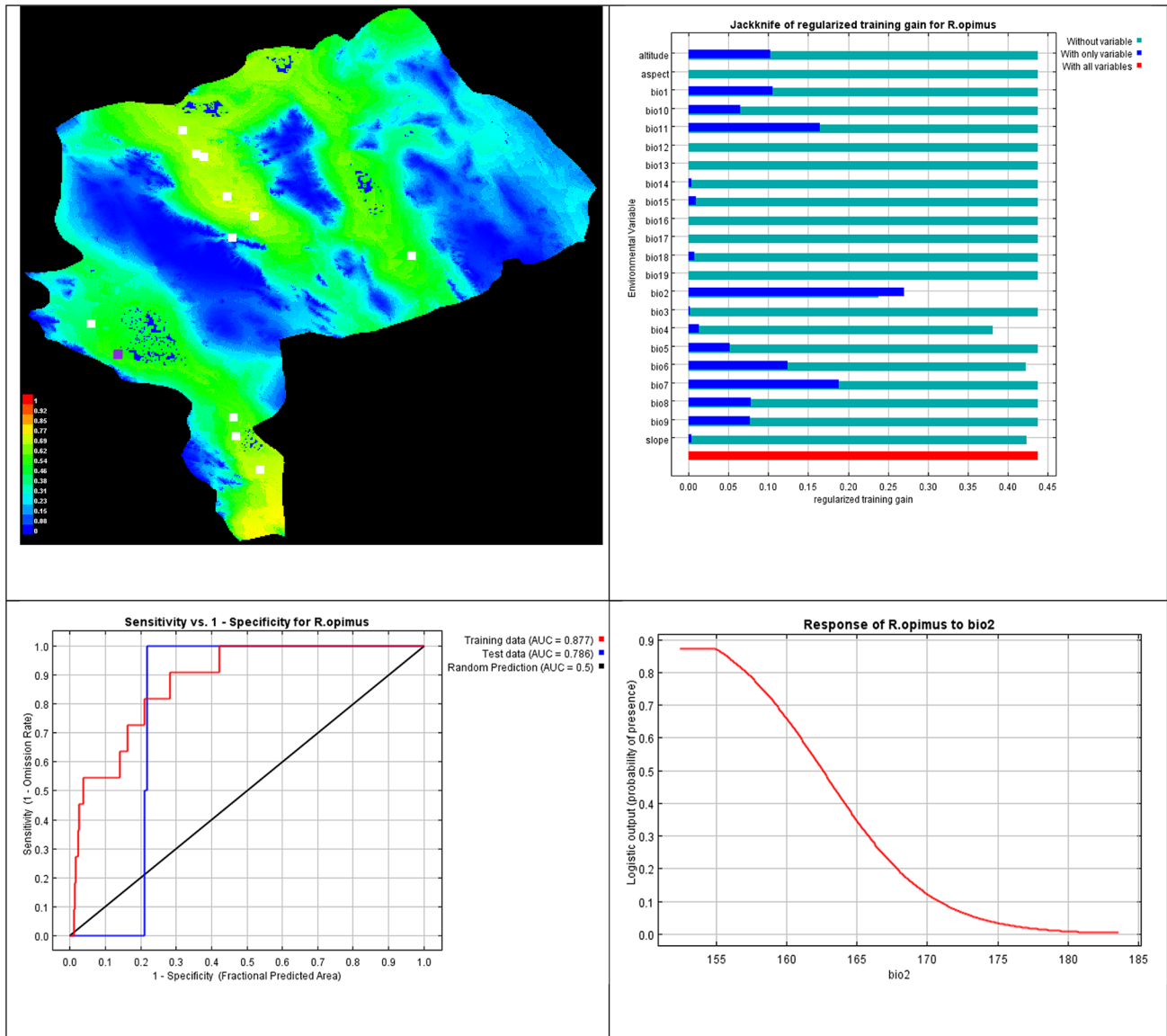


Fig. 3 Result of Maxent model and jackknife test for *R. opimus* in province of Yazd, Horizon 2050, RCP 4.5 scenario, and ACCESS1-0 Model

other variables, this variable has the most useful information (Fig. 4). The AUC for *R. opimus* was 0.851. The Jackknife test for *R. opimus* illustrated that BV 7 as the important environmental variable has the main gain when used in isolation. Therefore, it seems that this variable alone has the most useful information. So that the BV 7 was the variable that reduced the most gain when removed from the model. So, therefore, it seems unlike the other variables, this variable has the most useful information (Fig. 5).

Discussion

The extent of global climate change is worrying, and vector-borne diseases are sensitive to change of climate (Carvalho et al. 2017). Climate change has been associated with changes in behavior, distribution, density, and monthly activity of reservoirs and vectors of various disease including leishmaniasis (Mills et al. 2010). Predicting

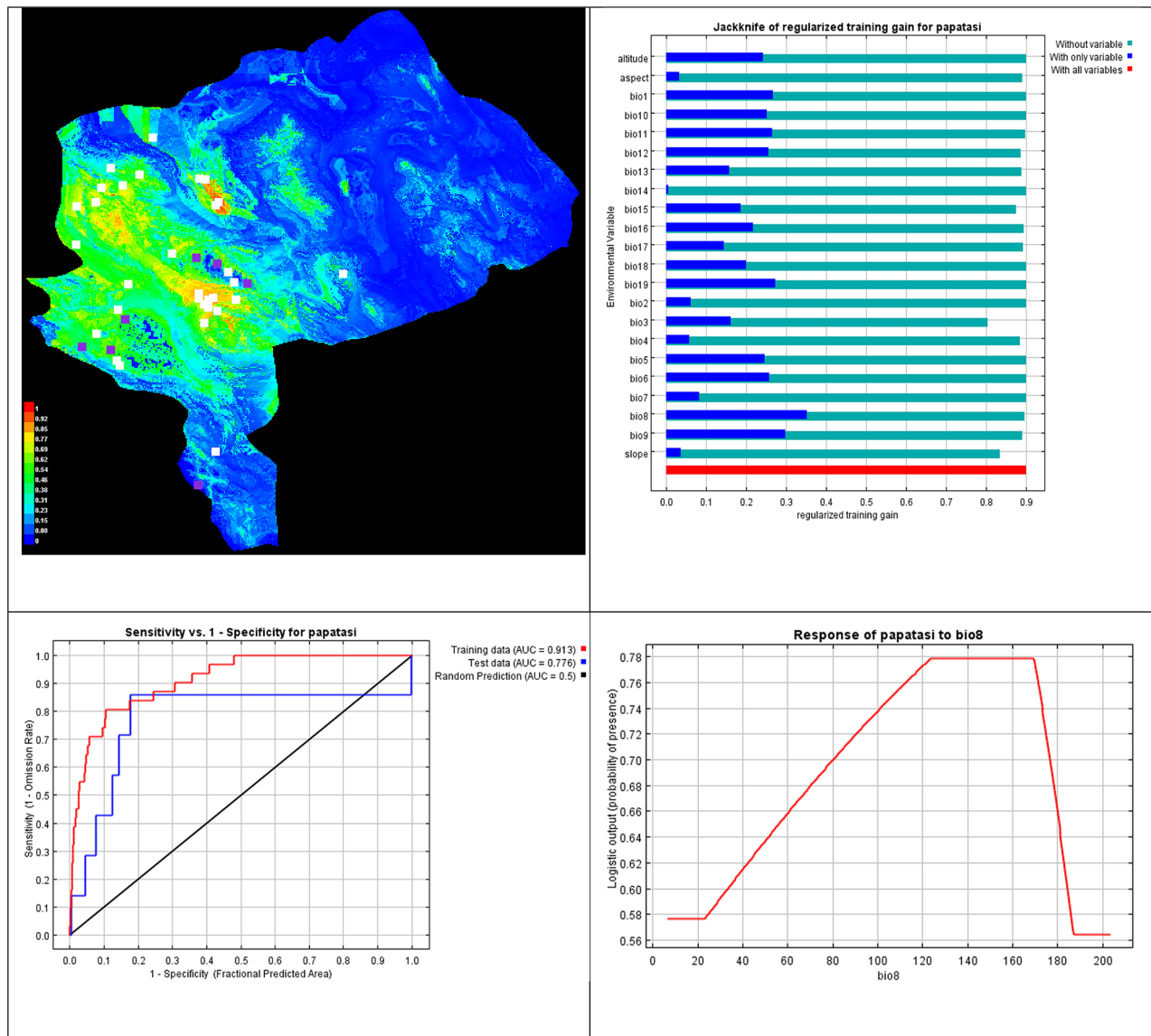


Fig. 4 Result of Maxent model and jackknife test for *P. papatasi* in province of Yazd, Horizon 2050, RCP 8.5 scenario, and ACCESS1-0 Model

the dispersion and outbreak of reservoirs and vectors in endemic foci of diseases is a challenge that disease control programs have to overcome in order to execute control interventions and to devise suitable climate change adaptation strategies. *L. major* is responsible for most of the cases of ZCL in Yazd province, and *R. opimus* and *P. papatasi* are the main reservoir host and vector of this parasite in the area, respectively. The present study predicted the climatic suitability of these species in the Yazd province of Iran in Horizon 2050. In our study, the AUC values for *R. opimus* distribution model were 0.87 and 0.85 under RCP 4.5 and 8.5 scenario (ACCESS1-0 Model), respectively. These values show the excellent prediction of the model. In another study conducted in

these province, the calculated AUC values for *R. opimus* were 0.91 and 0.96 under RCP 4.5 and 8.5 scenario (ACCESS1-0 Model), respectively (Shiravand et al. 2018). So, the results of this study were consistent with our study. The AUC values for *P. papatasi* were 0.92 and 0.91 under RCP 4.5 and 8.5 scenario (ACCESS1-0 Model), respectively. These values also confirm the excellent prediction of the model. The values of AUC obtained in several studies on this species throughout the world were between 0.90 and 0.99 (Abdel-Dayem et al. 2012; Colacicco-Mayhugh et al. 2010; Hanafi-Bojd et al. 2015; Shiravand et al. 2018; Sofizadeh et al. 2016), and in another study conducted in this province, the AUC was 0.91 (Shiravand et al. 2018). In Colombia, the AUC for *Lutzomyia evansi* was 0.88 and

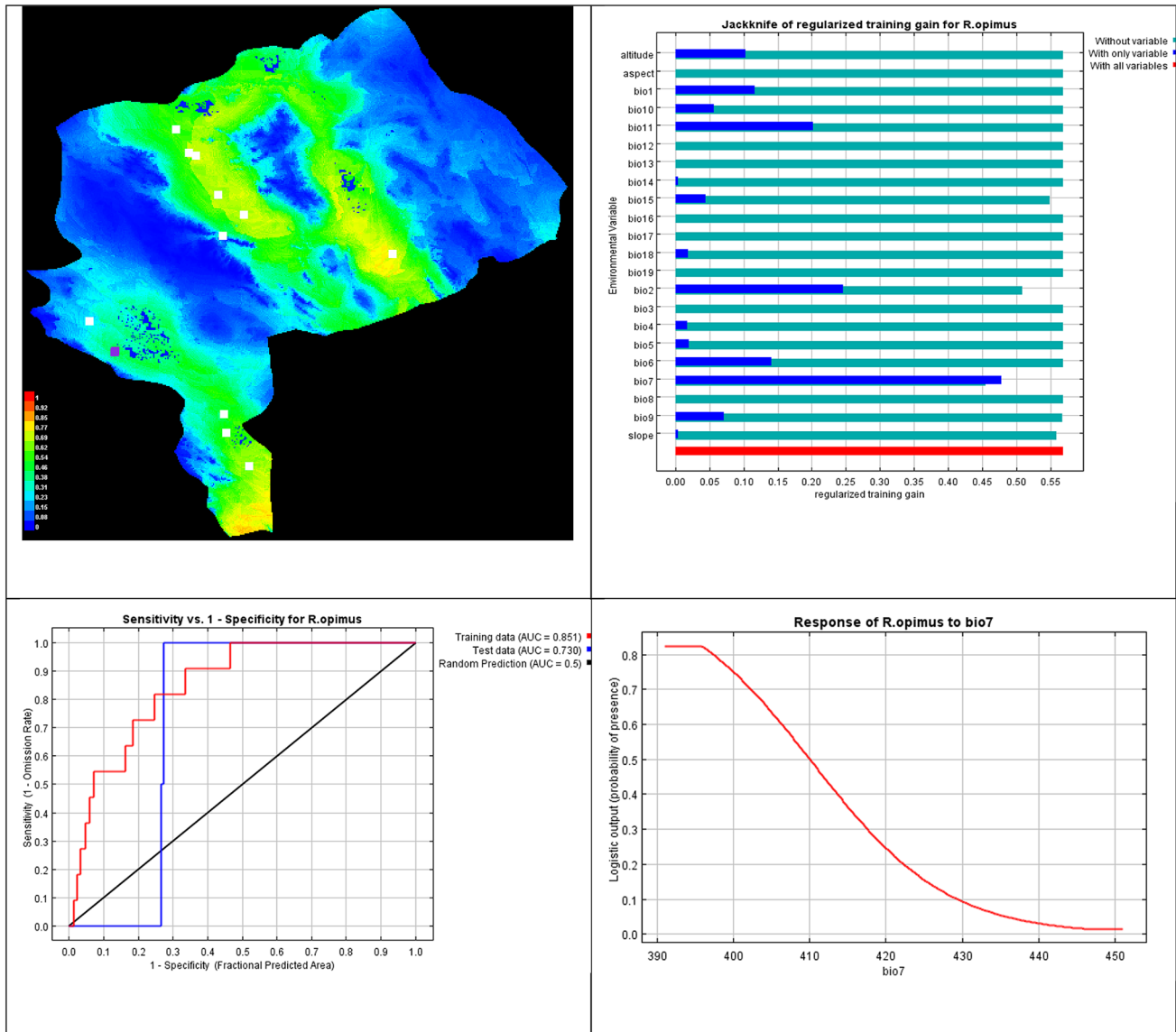


Fig. 5 Result of Maxent model and jackknife test for *R. opimus* in province of Yazd, Horizon 2050, RCP 8.5 scenario, and ACCESS1-0 Model

0.96 for *L. longipalpis* (González et al. 2014). By examining the AUC values obtained in our model and comparing them with those of other studies conducted in Iran and the world, we could conclude that the prediction made for the distribution of both species for the year 2050 in our study is acceptable and verifiable.

A study conducted in this province showed that the presence probability of *P. papatasi* in the western areas of this province is higher than in the other areas (Shiravand et al. 2018). Similar to this finding, future projections from our models indicate that the climatically suitable area for *P. papatasi* would expand to mainly westward areas of Yazd Province in the 2050s, and conversely, would decline in the eastern regions (Bafq County). The current reported presence probability of this species in Bafq County is about 70%

(Shiravand et al. 2018). It is projected that in the 2050s, many areas in the province would have a dramatic decline in ZCL distribution. Researchers in Europe have warned that climate change in the Eastern Mediterranean region in future years may favor an increased distribution of Leishmania vectors in these areas, and possibly increase the presence of the disease in the region (Medlock et al. 2014; Ready 2010). A research conducted in Ecuador displayed that in the 2030–2050s, Leishmania risk in the Andes Mountains would increase, and by the year 2100, the Andes Mountains will provide more suitable climate conditions for the distributions of sand flies (Escobar et al. 2016). By comparing the distribution map of *R. opimus* under the current climate (Shiravand et al. 2018) with the prediction map of this species in this study, we forecast that in the 2050s, *R. opimus*

will be distributed in more areas in Yazd province, and the probability of its presence would increase in the central and western regions of the province.

A study in the America has predicted that in the future, the distribution and cases of *Leishmania* would expand to the north of the continent, and by 2080, cases in these areas will be at least doubled (González et al. 2010). The latest report from the International Council for Science and Climate Change shows that climate changes would exacerbate human health problems, which poses a threat to public health (Field 2014; Woodward et al. 2014). *Leishmania* are highly sensitive to climate changes. The distribution and behavior of the vectors of *leishmania* are affected by climate changes including rainfall, temperature and wettest quarter (WHO 2010; Ready 2008). The results of our study showed that by 2050 temperature changes will have a higher contribution to the distribution of *P. papatasi*. Based on the results of Maxent modeling and Jackknife analysis, in the 2050s, BV 8, BV 9 and BV 7 will have the most effect on the distribution of *P. papatasi* in the province. Also, according to the analysis of variables contribution, this species seems to be very sensitive to the variation of temperature, because, the contribution of BV 8 in the model under RCP 4.5 and 8.5 scenarios were 38.1 and 34.6%, respectively, and these values were the highest in terms of variable contributions. In addition, according to the analysis of permutation importance, BV 3 (isothermality) ranked second under RCP 4.5 and 8.5 scenarios (Table 1 and Figs. 2, 4). Also, there was direct association between the distribution of *P. papatasi* and mean temperature of wettest quarter variable (BV 8) under RCP 8.5 scenario and ACCESS1-0 Model (Fig. 4). According to estimates by 2100, the mean global temperature would rise between 1.0 and 3.5 °C (Githeko et al. 2000). Therefore, we predict that the increase in the distribution of *P. papatasi* by 2050 in the Yazd Province will be due to the possible increase in air temperature, which will have a major impact on the distribution of this species. The importance of temperature in the distribution of *P. papatasi* also has been proven in other studies. so that Similar to the results of this study and the other studies conducted in Yazd province, the mean temperature of the wettest quarter (BV8), and in Golestan Province annual mean temperature were identified as the most important factors in the distribution of this species (Hanafi-Bojd et al. 2015; Shiravand et al. 2018; Sofizadeh et al. 2016). Also, the results of this study confirm the findings of Cross and Hyams (1996). However, in Europe, where *L. infantum* vector species are distributed in the Mediterranean and Temperate BVmes. It is also reported that temperature is the main restricting factor for sandflies distribution, probably forcing insect diapause in cold months (Fischer et al. 2010; Ready 2010). A study on the probability of *P. papatasi* distribution in Libya using the MaxEnt model showed that annual rainfall was the most

important factor, and temperature and elevation had the least effect on the model, which is inconsistent with our findings (Abdel-Dayem et al. 2012). In this study, according to the analysis of variable contributions, precipitation of wettest month was the third important variable. While precipitation seasonality was found to be the fourth most important variable under RCP 4.5 and RCP 8.5, respectively. A study conducted in Colombia showed that the distribution of the two *L. infantum* vector species *L. longipalpis* and *L. evansi* in the environment is strongly correlated with precipitation (González et al. 2014).

The result of a study in Brazil showed that precipitation, more than temperature, is the variable regulating local abundances of *L. longipalpis* populations (Queiroz et al. 2012). Similar to the distribution of *P. papatasi*, in the 2050 s, the temperature will also have the most effect on the distribution of *R. opimus*. The results of Jackknife test showed that in the 2050s, BV 7, BV 2 and BV 11 would have the highest effect on the distribution of *R. opimus*. According to the analysis of variable contributions, *R. opimus* seem to be very sensitive to variations in temperature. For this species, two temperature variables contributed almost 93.4% to the model; variables which contributed the most include mean diurnal range (BV 2 = 76.7%) followed by temperature seasonality (BV 4 = 16.7%) under RCP 4.5 scenario. Under RCP 8.5 scenario, the variables which contributed the most are temperature annual range (BV 7 = 73.5%) followed by mean annual range (BV 2 = 21.5%). In addition, according to the analysis of permutation importance, temperature annual range (BV 7), mean diurnal range (BV 2) and temperature seasonality (BV 4) were the most effective variables under both RCP 4.5 and 8.5 scenarios. In a study conducted in Iran (Gholamrezaei et al. 2016), slope, mean temperature of coldest quarter (BV 11), annual mean temperature (BV1), and mean temperature of wettest quarter (BV 8) were identified as the most important variables on the distribution of *R. opimus*. A study in conducted Golestan Province of Iran, identified altitude, NDVI, soil type, and climate as the most important factors that contribute to habitat suitability and geographical distribution of *R. opimus* in this province (Ahmadpour et al. 2018).

Conclusion

In recent decades, factors such as drought, the planting of certain plants such as Haloxylon and Atriplex around cities and villages to stabilize sandy soils, and the unauthorized use of groundwater for the development of agriculture around villages and cities play an important role in the growth and convergence of rodent colonies in areas of human settlement. This increases the chance that these rodents get closer to human settlements to find food and

shelter. This also increases the exposure of the rodents to *P. papatasi* which feeds on the reservoir rodents and contaminate humans through biting.

Climate factors have a major influence on the spatial distribution of ZCL in Yazd Province. These findings can provide essential basis for public health policy makers to monitor and forecast the disease dynamics based on the climate projections for future control strategies. This means that appropriate personnel, budget and resources should be allocated more efficiently by concentrating on the major determinants of ZCL epidemiology in Yazd Province.

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Compliance with ethical standards

Conflict of interest None.

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