

Original Article

Predicting the Potential Distribution of Major Malaria Vectors Based on Climate Changes in Sistan and Baluchistan Province, Southeastern Iran

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Abstract

Background: Given the significance of climate change and its substantial effects on mosquitoes' habitats, this study was aimed to model the spatial distribution of the main malaria vectors in the south east of Iran.

Methods: Several scientific databases between 1980 and 2019 were reviewed to find mosquito species and their spatial information in this area. The archived folders in the center for diseases control and prevention were used to exploit essential data on malaria cases and foci. Three representative concentration pathways (RCP2.6, RCP4.5 and RCP8.5) were chosen to stand for three possible climate scenarios. Finally the potential species distribution of *Anopheles stephensi* and *An. culicifacies* s.l. in the 2030s and 2050s horizons were estimated by the Maximum Entropy Model.

Results: So far, a total of 39 mosquito species belonging to the family Culicidae have been reported from the study area. In 2019, the total malaria cases have increased by 91% compared to 2015, as well as a sharp rise than 2018 (249%). In that year, 91% of cases were imported from other countries, which caused 40% increase in the new potential foci than in 2018. The Jackknife test demonstrated the annual mean temperature and precipitation of the coldest quarter with the greatest impact on the environmental suitability of the mentioned two species.

Conclusion: The effect of climate change on the appearance and recurrence of mosquito-borne diseases has been demonstrated in various studies. Collecting further data and conducting investigation on this issue will improve control management, especially for the malaria vectors.

Keywords: Malaria; Maximum entropy model; *Anopheles*; Iran

Introduction

Mosquitoes are the most important organisms affecting humans' health and even social-economic development (1). Biting, persistent annoyance, along with their significant role in the transmission of a variety of diseases, has made them dangerous vectors. Malaria, dengue fever, West Nile,

Rift Valley fever, Chikungunya fever and Yellow fever are some vector-borne diseases transmitted by mosquitoes (2).

Malaria is one of the most common tropical mosquito-borne infections in the world. The World Health Organization reported about 229 million cases of infection

and 409,000 deaths in 2019 were related to this disease (3). Mosquitoes of the genus *Anopheles* are the vectors of this parasitic disease. So far 465 *Anopheles* species have been identified, about 70 of which can transmit human malarial protozoa, yet 41 species are known as dominant vectors. *Anopheles superpictus* s.l., *An. sergentii*, *An. sacharovi*, *An. subpictus*, *An. stephensi*, *An. fluviatilis* s.l., and *An. culicifacies* s.l. are some of major malaria vectors in the Europe/Middle-East and Asia region (4).

Although most parts of Iran are “Anophelism without malaria”, southern and southeastern parts of the country are still faced with this disease. Thus, four-fifths of cases belong to the two provinces of Hormozgan and Sistan and Baluchistan. Despite the successful implementation of malaria elimination program in Iran, these areas continue to report indigenous malaria cases. Sistan and Baluchistan Province has the most malaria cases and the highest number of its vectors in the country (5). According to the statistics of the malaria office, Center for Disease prevention and control (CDC), a total of 2036 cases occurred in Sistan and Baluchistan during 2015–2019. Although the total malaria cases have declined significantly until 2017, it has been increasing since then. It is obvious; those non-Iranian and imported cases have grown considerably. In that year, 91% of cases were imported from other countries, which caused a 40% increase in the new potential foci than in 2018 (6). These patients were mainly immigrants from Pakistan and Afghanistan, the countries neighbored with Sistan and Baluchistan Province. According to the world malaria report 2020, there were 173860 and 413533 indigenous cases in Afghanistan and Pakistan in 2019 (3). Fortunately, no indigenous cases have been reported, along with the slight growth of clear up (3%) and a reduction on the residual active foci (-16%) in Sistan and Baluchistan Province since 2019 (6).

Based on the last checklist of Iranian mosquitoes, the Culicidae family includes 70 species classified in 8 or 12 genera (7,8).

Five of seven Iranian malaria vectors exist in this province: *Anopheles culicifacies* s.l., *An. stephensi*, *An. fluviatilis* s.l., *An. dthali*, and *An. superpictus* s.l. In addition, *An. pulcherrimus* is known as a potential vector of malaria in this region. The first three species are considered more important in the malaria transmission and outbreak (9). Nevertheless, there is no comprehensive report on mosquito composition in the southeast of Iran.

It seems climatic conditions have a key role in the appearance and establishment of these vectors in this Oriental Ecozone (10-11). Global warming along with environmental changes and precipitation can lead to the emergence and survival of *Anopheles* mosquitoes (12). Therefore, knowing the distribution of malaria vectors in the future is important for the health care system, especially with respect to the malaria control strategic plan in this region (9).

Predictive habitat distribution modeling has been increasingly used in recent years to study disease vectors. It exploits computer algorithms to discover fundamental niches of organisms and regards environmental and climate data as independent variables. Hence, this method could help understand how environmental conditions lead to the appearance or growth of a species. Furthermore, it could be used to explore both a species' future distribution within certain climate change situations and the possible future distribution of an invasive species. A number of recent studies around the world have adopted this method to investigate malaria vectors (13-14). Species distribution models (SDM) are being used to predict the distribution of vectors of vector-borne diseases. One model that has been widely used in this regard in recent years is the MaxEnt model. In other words, studies on vectors and reservoirs of vector-borne diseases in Iran and other countries have been performed by this model (15-19).

Given the significance of climate change and its substantial effects on mosquitoes' habitats, this study was aimed to establish a database on mosquitoes' composition

and to model the spatial distribution of the main malaria vectors in the 2030s and 2050s horizons.

Materials and Methods

Study area

This study was conducted in Sistan and Baluchistan Province (also called Sistan and Baluchestan or Sistan-Baluchestan), the second largest province in Iran. Located in the southeast of the country, it borders Afghanistan and Pakistan to the east and the Oman Gulf and the Indian Ocean to the south (Fig. 1). It has an area of about 181,785 km² and a population of approximately 2,534,327 people with 1.05% annual growth rate who live in 19 cities, 37 towns, and 9,716 villages. This province has a generally arid climate with dust storms and 120-day winds. On the other hand, there is a variety of climatic conditions due to seasonal subtropical high pressures, large interior deserts, the Alpine-Himalayan folded system, and the Jazmurian basin. Moreover, the vast seas in the south, Hirmand basin in the north, and periodic Monsoon winds contribute to the development of ecological diversity in the province. The humidity in the south areas is largely due to Bangal Gulf streams, which reach summer rainfall as a rare event in Iran (20).

Data collection (species data)

Several scientific databases (Google Scholar, PubMed, SID, Ovid Medline, Web of Science, IranDoc, and Magiran) were reviewed to find all articles and dissertations published in English and Persian languages between 1980 and 2019 on mosquitoes' species and ecology in Sistan and Baluchistan Province. The following keywords were searched: “*Anopheles*”, “*Culex*”, “*Aedes*”, “*Culiseta*”, “*Uranotaenia*”, “*Ochlerotatus*”, “*Anopheles stephensi*”, “*Anopheles culicifacies*”, “mosquito”, “Culicidae”, “fauna”, “Sistan and Baluchistan”. The inclusion criteria were all data with information on the fauna of mosquitoes as well as spatial information (coordinates of collection sites)

about *An. stephensi* and *An. culicifacies* s.l. Exclusion criteria were all documents were published in languages other than English and Persian and did not contain information about the distribution of mosquitoes in Sistan and Baluchistan Province. Figure 2 shows the strategy of search in this study.

Environmental and bioclimatic data

The WorldClim database with 1 km² spatial resolution (<http://www.worldclim.org/bioclim.htm>) was used for current bioclimatic data as well as data predicted for the 2030s and 2050s (Table 1).

Modeling and mapping ecological niche modeling in different time intervals

Using ArcGIS 10.3, we clipped all environmental and weather variables to the border of Iran (analysis mask). Then, the variables were converted to ASCII format for modeling in the next step based on the maximum entropy Model (MaxEnt), version 3.4.1. This model estimates potential species distribution by considering existing records of a given species and environmental layers. The model randomly divided the occurrence data of each species into training (80%) and testing (20%) subgroups. The area under the receiver operating characteristic curve (AUC) shows the performance of the model. Accordingly, higher AUC values were interpreted as better model predictions. An AUC above 0.75 can be reasonably used. If AUC values in a model approximate 1, we will have a better model. Jackknife analysis was employed to examine the contributions of both environmental and bioclimatic variables (21).

Totally, the presence records used for training and test of the model were 58 and 14 for *An. culicifacies* s.l. and 46 and 11 for *An. stephensi*. The background points used in modeling were 10,054 and 10,043 for *An. culicifacies* s.l. and *An. stephensi*, respectively.

Three representative concentration pathways (RCPs) (RCP2.6, RCP4.5, and RCP8.5) were chosen to stand for three possible climate scenarios. The RCP2.6 concentration scenario

suggested very low levels of greenhouse gas concentration (2.6 W/m²) that are thought to raise the global mean temperature to 2 °C (22). RCP4.5 is a stabilization scenario where total radiative forcing is stabilized a few years after 2100, but there is no sign of going beyond the long-run radiative forcing target (23). Finally, RCP8.5 is characterized by the gradual rise in greenhouse gas emissions and, as a result, concentration levels (24). We then used the data of future climate scenarios to run the model in order to estimate the spatial distribution of the most suitable ecological niches for each malaria vector species over two time periods; the 2030s and 2050s.

Results

Checklist of mosquitos in Sistan and Baluchistan Province, Iran

So far, the following 39 mosquito species belonging to the Culicidae family have been reported from the study area (Table 2).

Ecological niche modeling

Using three climate change scenarios (RCP2.6, RCP4.5, and RCP8.5) in the 2030s and 2050s, we discuss the environmental suitability (ES) of two malaria vectors in the

south east of Iran.

Suitable distribution areas of *An. culicifacies* s.l. and *An. stephensi* are illustrated in the obtained maps (Fig. 3). The probability of the geographical distribution of each species varied between 0 (blue color) and 1 (red color). The white and violet points, respectively, indicate training locations (80%) and test locations (20%).

Prediction of ecological niches in the 2030s *Anopheles culicifacies* s.l.

The range of this vector is limited to the southern areas of the province, in particular the central parts. Figure 3 exhibits the prediction maps of *An. culicifacies* s.l. under the three climate change scenarios. Under RCP2.6, the predicated AUC was respectively 0.881 and 0.805 for training and test data. Under RCP4.5, this value was 0.886 and 0.807 for training and test data, respectively; and under RCP8.5, it was 0.880 and 0.807 for training and test data, respectively. The Jackknife test showed bio1 as the highest value among environmental variables for RCP2.6 and RCP4.5. In the case of RCP8.5, bio19 had the highest value (Figs. 4 and 5). The environmental variables whose exclusion caused the

Table 1. Bioclimatic variables used in the model

Variable	Description
Bio1	Annual mean temperature (°C)
Bio2	Mean diurnal range: mean of monthly (max temp–min temp; °C)
Bio3	Isothermality: (Bio2/Bio7) × 100
Bio4	Temperature seasonality (SD × 100)
Bio5	Maximum temperature of warmest month (°C)
Bio6	Minimum 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)

highest reduction in AUC were bio3, bio14, and bio3 for RCP2.6, RCP4.5, and RCP8.5 scenarios, respectively.

Anopheles stephensi

This species as the main malaria vector in Iran was associated with the most suitable ecological niches in the central areas of Sistan and Baluchistan Province, especially southern parts. The activity of this species was mainly found in the coastal areas (Fig.

3). In the RCP2.6 scenario, the AUC was 0.897 and 0.875 for training and test data, respectively. In the RCP4.5 scenario, this value was 0.903 and 0.815 for training and test data, respectively. Finally, in the RCP8.5 scenario, it was 0.900 and 0.815 for training and test data, respectively. Regarding the significance of variables, Jackknife test indicated that bio1 was the most important under all scenarios if used independently (Figs. 4 and 5). On the other hand, the

Table 2. Checklist of mosquitos in Sistan and Baluchistan Province, southeastern Iran

Subfamily	Genus	Subgenus	Species	Reference	
Anophelinae	<i>Anopheles</i>	<i>Anopheles</i>	<i>peditaeniatus</i>	(6)	
		<i>Cellia</i>	<i>apoci</i>	(40)	
			<i>dthali</i>	(41)	
			<i>culicifacies</i> s.l.	(42)	
			<i>fluviatilis</i> s.l.	(42)	
			<i>pulcherrimus</i>	(42)	
			<i>stephensi</i>	(42)	
			<i>moghulensis</i>	(42)	
			<i>sergentii</i>	(42)	
			<i>turkhudi</i>	(43)	
			<i>multicolor</i>	(43)	
			<i>superpictus</i> s.l.	(10)	
			<i>subpictus</i> s.l.	(10)	
Culicinae	<i>Aedes</i>	<i>Aedimorphus</i>	<i>vexans</i>	(44)	
		<i>Stegomyia</i>	<i>unlineatus</i>	(45)	
	<i>Ochlerotatus</i>	<i>Ochlerotatus</i>	<i>albopictus</i>	(46)	
			<i>caballus</i>	(46)	
			<i>flavescens</i>	(46)	
			<i>caspius</i>	(46)	
	<i>Culex</i>	<i>Barraudius</i>	<i>pusillus</i>	(45)	
			<i>Culex</i>	<i>pipiens</i>	(45)
				<i>quinquefasciatus</i>	(45)
				<i>perexiguus</i>	(45)
				<i>theileri</i>	(45)
				<i>laticinctus</i>	(45)
				<i>sinaiticus</i>	(45)
				<i>sitiens</i>	(45)
				<i>mimeticus</i>	(45)
				<i>tritaeniorhynchus</i>	(45)
				<i>pseudovishnui</i>	(47)
			<i>Neoculex</i>	<i>territance</i>	(49)
	<i>Maillotia</i>		<i>arbieeni</i>	(47)	
			<i>deserticola</i>	(47)	
<i>hortensis</i>			(47)		
	<i>Oculeomyia</i>	<i>bitaeniorhynchus</i>	(44)		
<i>Culiseta</i>	<i>Allotheobaldia</i>	<i>longiareolata</i>	(48)		
<i>Uranotaenia</i>	<i>Pseudoficalbia</i>	<i>unguiculata</i>	(44)		
<i>Mansonia</i>	<i>Mansonia</i>	<i>uniformis</i>	(8)		

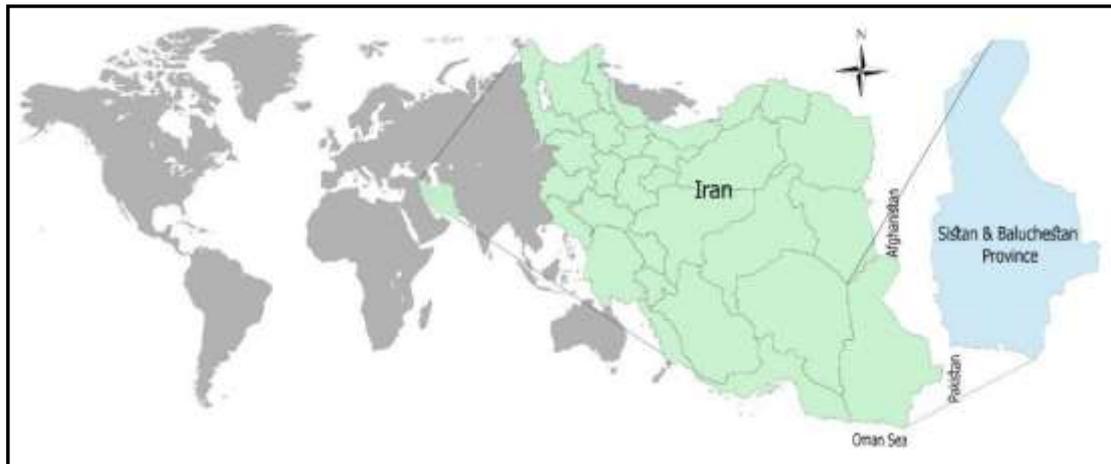


Fig. 1. The study area; Sistan and Baluchistan Province, southeastern Iran

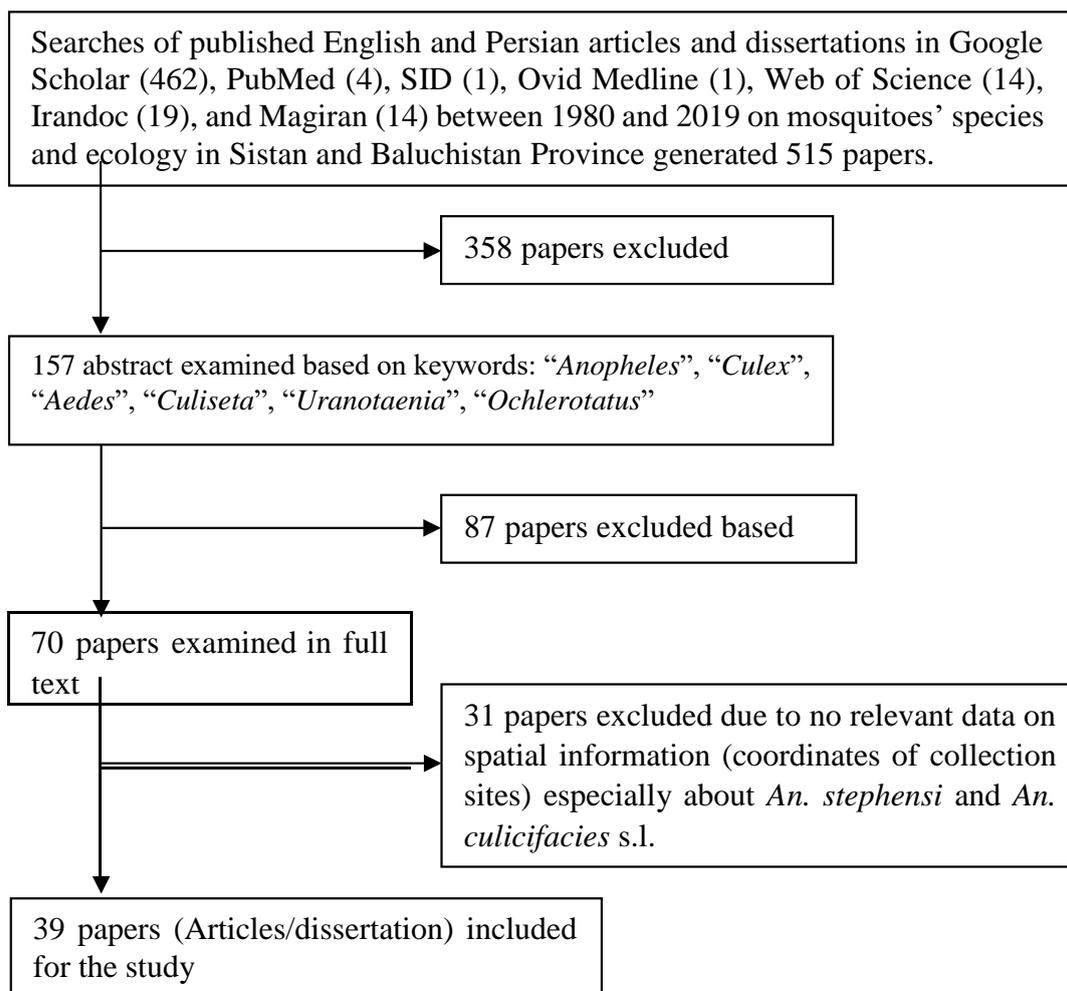


Fig. 2. Flow chart of search strategy

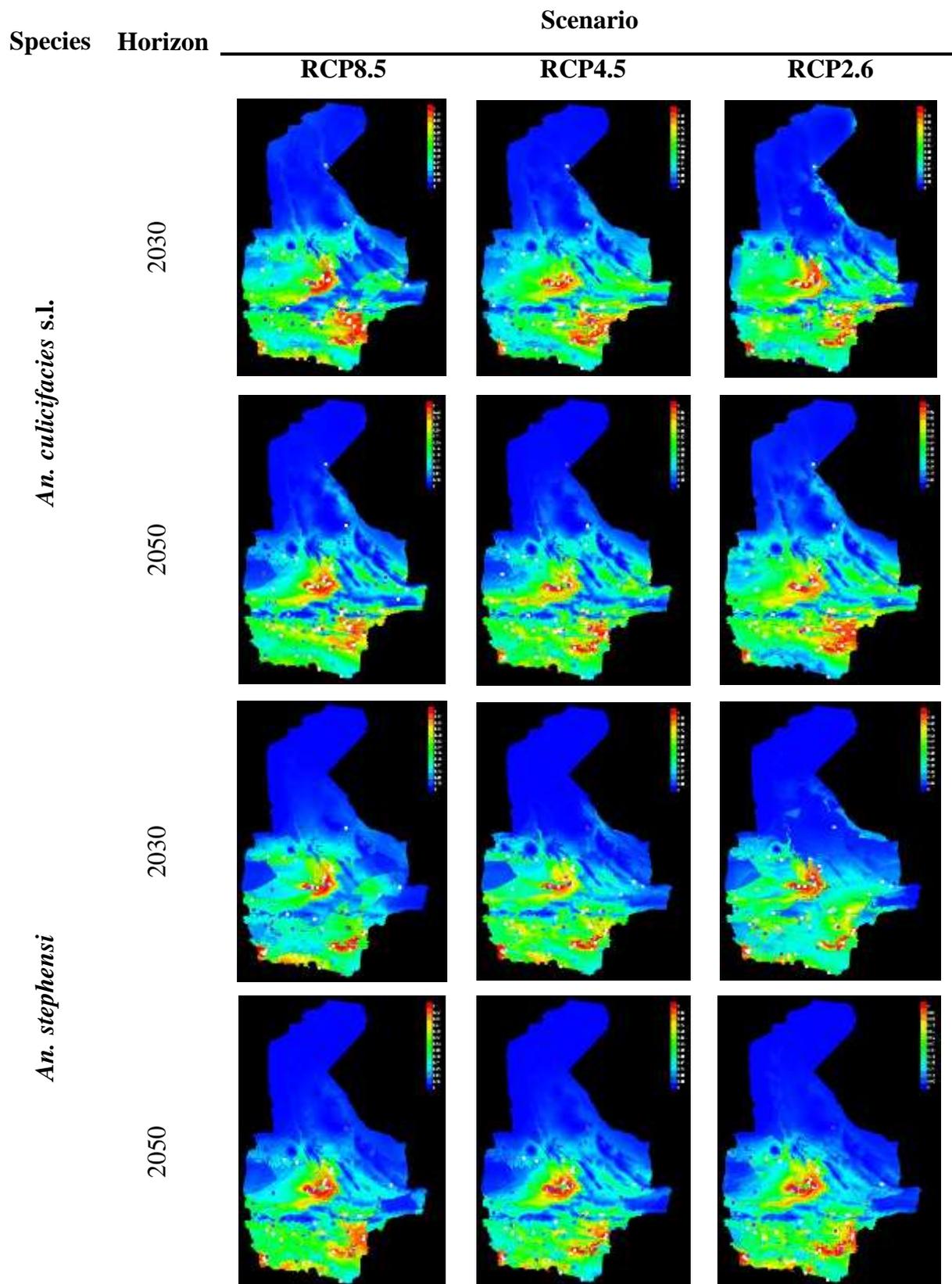


Fig. 3. Environmental suitability for two malaria vectors in southeast of Iran under three climate change scenarios in 2030s and 2050s

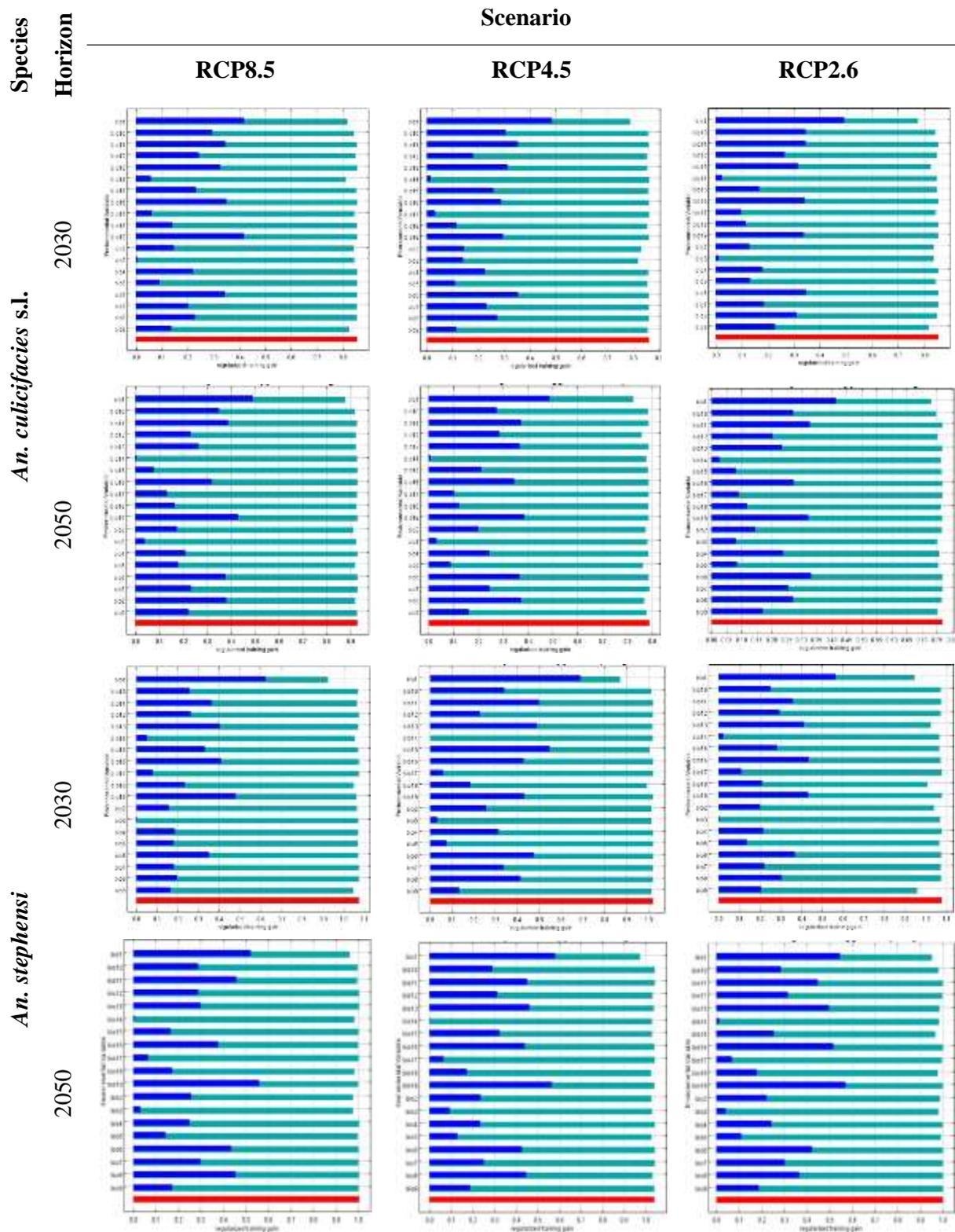


Fig. 4. The results of Jackknife test for two malaria vectors in southeast of Iran in the 2030s and 2050s

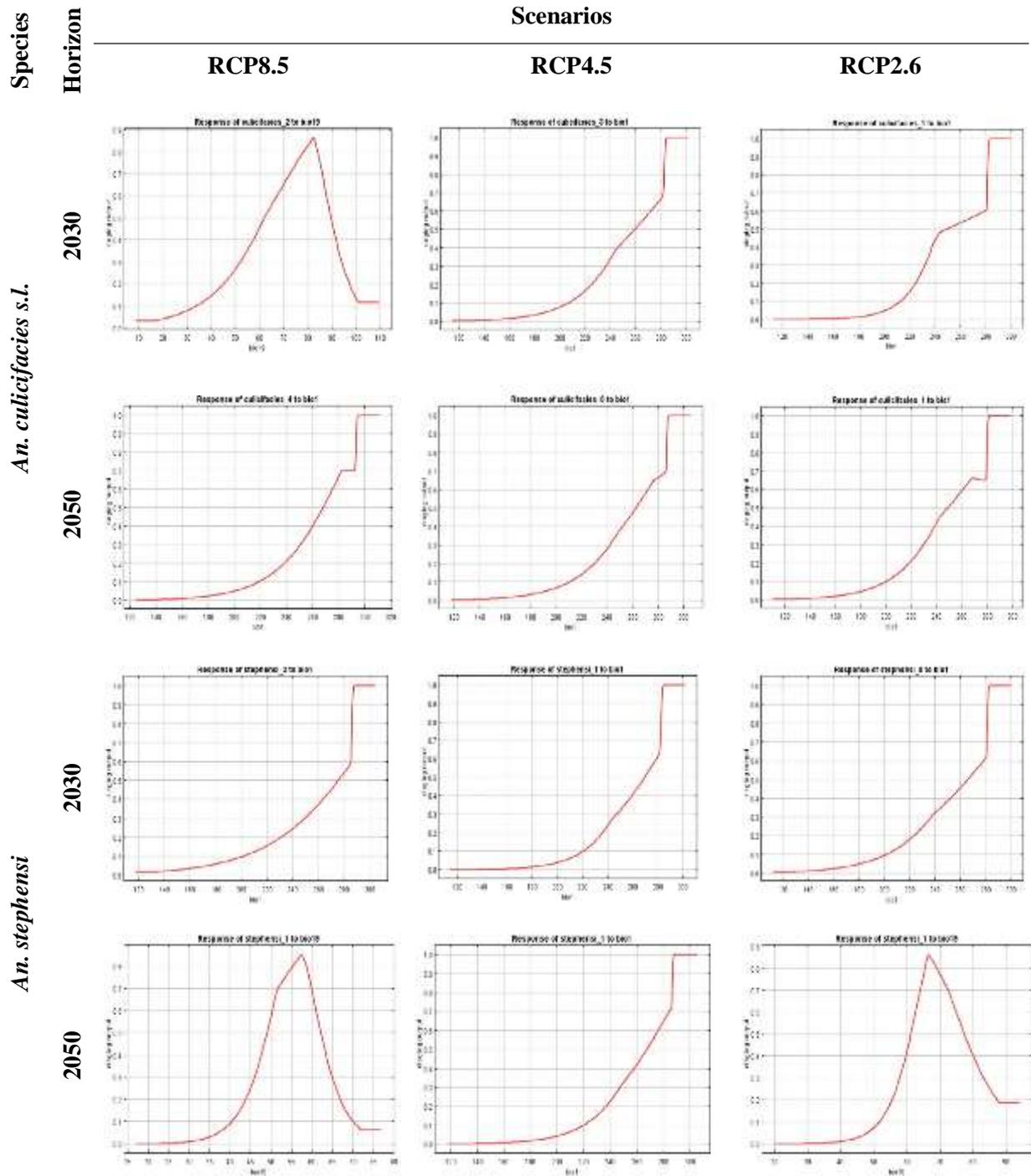


Fig. 5. The most effective variable on the modeling of two malaria vectors in southeast of Iran in the 2030s and 2050s

environmental variables whose removal led to the highest reduction in AUC were bio3, bio14, and bio3 for RCP2.6, RCP4.5, and RCP8.5 scenarios, respectively.

Prediction of ecological niches in the 2050s

In this section, the results of the MaxEnt model for the related malaria vectors are given according to climate change scenarios

in the 2050s (Figure 3). The variations between the study scenarios and time periods are discussed in the following paragraphs.

Anopheles culicifacies s.l.

Under the RCP2.6 scenario, the AUC was 0.858 and 0.826 for training and test data, respectively. The estimated AUC for the RCP4.5 scenario was 0.876 and 0.836 for training and test data, respectively. Under the RCP8.5 scenario, the AUC was 0.875 and 0.781 for training and test data, respectively. The Jackknife test of variable importance suggested bio1 to have the highest value if considered independently under all scenarios (Figs. 4 and 5). The environmental variable whose removal caused the highest reduction in AUC was bio14 under all scenarios.

Anopheles stephensi

Under the RCP2.6 scenario, the AUC was 0.908 and 0.795 for training and test data, respectively. The AUC under the RCP4.5 scenario was 0.903 and 0.806 for training and test data, respectively. Under the RCP8.5 scenario, this value was 0.904 and 0.815 for training and test data, respectively. The Jackknife test demonstrated that the environmental variables with the greatest value if used independently were bio19 under RCP2.6 and RCP8.5 scenarios and bio1 under RCP4.5 scenario (Figs. 4 and 5). Eventually, under all scenarios, bio14 was shown to be the environmental variable whose elimination caused the highest reduction in the AUC.

Discussion

Southeastern Iran still has the highest number of malaria cases in the country. The significant reduction in malaria cases demonstrates Iran's success in this program, but the sudden increase in cases in 2019 along with the rise in the number of cleared-up foci could be alarming. Malaria pre-elimination program was launched in Iran with the support of WHO in 2009. It aimed at stopping the spread of *P. falciparum* and freeing Iran from malaria by the end

of 2015 and 2025, respectively. In such a situation, imported malaria is as worrying as indigenous cases (5). In recent years, non-Iranian and imported cases have grown considerably. A study in the south of Iran indicated that the presence of foreigners could lead to the outbreak of malaria and, thus, alter the classification of cleared up and potential foci (25). Along with the prevalence of *P. vivax* in Iran, this issue can further highlight the need to estimate the distribution of mosquito species. This is in view of the fact that early occurrence of malaria gametocytes, transmission by *Anopheles* vectors at lower parasite densities and faster growth of sporozoites within the mosquito contribute to the re-emergence or survival of malaria in an area (26).

Because of its special climatic conditions, southeastern Iran has a suitable environment for mosquitoes to breed. In addition, it is possible for vectors of various diseases, including malaria and dengue fever, to enter the province owing to the long natural border (20). Reviewing the literature showed that this vast region of the country is home to 39 species of the family Culicidae identified in the form of five genera. Some authors have distinguished the genus *Ochlerotatus* from *Aedes*, but recent studies have classified it as a subgenus of *Aedes* (27, 28).

Many of the species reported in the results of our study, including *Cx. pipiens*, *Cx. theileri*, and *Ae. caspius* s.l., are among the potential or proven vectors of some pathogens associated with human and domesticated animals around the world (29). In this regard, the two species of *An. culicifacies* s.l. and *An. stephensi* are the main vectors of malaria.

Species diversity in the eastern neighboring countries, especially in the areas adjacent to the Iranian border, and its similarity with the species in southeastern Iran is remarkable. The key to the Anopheline mosquitoes of Pakistan recorded 24 species. The main malaria vector in Pakistan, particularly in the Punjab, North West Frontier Province, Sindh, Baluchistan, and the Karachi area, is *An. culicifacies* s.l. Giles.

Also *An. stephensi* and *An. superpictus* s.l. are suspected vectors in these areas (30). *Culiseta longiareolata* is another common species in Pakistan, Western Himalayas, Baluchistan, and Sindh (31). The suspected malaria vector in Iran, *An. pulcherrimus*, has widespread distribution, extending from Lebanon to Pakistan and Afghanistan (32). In a study on the composition of *Anopheles* species in malarious areas of Afghanistan and Iran, *An. hyrcanus*, *An. stephensi*, and *An. superpictus* s.l. were collected from the Afghan provinces of Herat, Nangarhar, and Kunduz (33). In oriental regions, including Sistan and Baluchistan, *An. subpictus* is another widely distributed species. It could be found in most parts of India during the rainy season. While it is not a malaria vector in Iran (11), sibling species A of *An. subpictus* (fresh water form) has been recorded as a major vector in West Bengal, India (34).

In the current critical situation where the country is in the eliminating malaria phase and in order to obtain the malaria elimination certificate, determining suitable habitats for important malaria vectors in the strategic region of Sistan and Baluchistan is of particular importance. Due to the presence of numerous immigrants from Afghanistan and Pakistan, the presence of malaria cases, especially asymptomatic patients in areas where malaria vectors can develop, is very dangerous and could make the malaria eradication program failure. According to the model, some areas potentially rife with malaria vectors in Sistan and Baluchistan Province are near the border, which is cause for concern because the country is still in the elimination phase of malaria. The endemic foci of malaria are currently limited to the southeastern parts of Iran. In recent years, *An. stephensi*, a strong malaria vector, has spread to new areas. This vector was first noted in Djibouti and Sri Lanka in the past decade (35-37). These studies can confirm that climate change has influenced the geographical distribution of some invasive vectors. This could negatively affect programs that aim to eliminate malaria globally.

In the present study, annual mean temperature (bio1) had the greatest impact on the environmental suitability (ES) of *An. culicifacies* s.l.; also, precipitation of the coldest quarter (bio19) had the greatest impact on the ecological niche of this species in the RCP8.5 scenario (2030s). Although, temperature seasonality (bio 4) followed by annual precipitation (bio12) was resulted as the biggest bioclimatic variables for *An. culicifacies* s.l. (9), it seems that the temperature and precipitation have the most important effect on ES of this species. Other studies have emphasized the role of the mean temperature of the coldest quarter (bio11). In a study modeling the ecological niche of this species, it was observed that the rise in bio11 could reinforce the ES of *An. culicifacies* s.l. in four scenarios between the 2030s and 2050s. But a drop in the precipitation of the warmest quarter and a precipitation seasonality ranging from 100 to 120 could amplify the ES for this vector (21). As in our study, some previous maximum entropy models regard precipitation of the driest month (bio14) as the environmental variable with a low effect on the ES of this species (9). It seems that precipitation in these months cannot increase the number of wetlands or their sustainability; therefore, it will not affect the reproduction of this species.

As in the case of *An. culicifacies* s.l., bio1 and, occasionally, bio19 were the most important variables for *An. stephensi* in some scenarios. Likewise, some other studies in Iran have reported bio15 followed by bio1 as the biggest contributors to the growth of ES of this species. The results of the Jackknife test regarding *An. stephensi* and *An. culicifacies* s.l. suggested that temperature and precipitation significantly affect the prediction power (9).

Researchers have also acknowledged the important role of precipitation of the coldest quarter on ES of *An. superpictus* s.l. under all scenarios (21). Laporta et al. in 2011 concluded that slope and land cover were the main bioclimatic parameters for *An. bellator* and *An. marajoara* (38). Also, altitude, stream vegetation, and soil as the most crucial

factors for improving potentially suitable niches for *An. sergentii* and *An. gambiae* were proposed by other researchers (39). It can show the difference in the impact of climate variables on the ES of each malaria vector in every area. It seems estimating and mapping the distribution of *Anopheles* based on spatial factors and environmental changes could be useful for those who provide careful planning and devise effective control policies for problematic areas (9). The effect of climate change on the appearance and recurrence of mosquito-borne diseases has been demonstrated in various studies (21). Collecting further data and conducting investigation on this issue will improve control management, especially for the malaria vectors.

The major limitation of this study was the failure of spatial information (coordinates of collection sites) for the Sistan and Baluchistan malaria vectors in some published documents. Due to the important role of geographical coordinates for further studies, its registration is recommended to researchers.

Conclusion

Although some countries have succeeded in eliminating malaria, this task seems more daunting in climatically diverse areas such as southeastern Iran, which features both Oriental and Palearctic realms. The main barriers to eliminating malaria are the lack of enough and reliable data about vectors, parasites, and their climatic preferences, excessive globalization and immigration, and global warming. In countries dealing with malaria elimination, studying the future of climate change and its impact on the spread of disease vectors can assist health decision-makers to develop more specific and effective targets for malaria control policies.

Vector control is an important part of the malaria elimination program, and GIS-based forecasting maps can be effective in realizing sustainable malaria control rather than temporary elimination. In addition,

conducting extensive studies on the impact of development infrastructure, social and economic indicators can help identify areas that need more attention so that the integrated vector management is correctly implemented or upgraded.

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Conflict of interest

The authors declare there is no conflict of interests.

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