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Predicting the potential distribution of main malaria vectors *Anopheles stephensi, An. culicifacies* s.l. and *An. fluviatilis* s.l. in Iran based on maximum entropy model

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ABSTRACT

Malaria is considered as a major public health problem in southern areas of Iran. The goal of this study was to predict best ecological niches of three main malaria vectors of Iran: *Anopheles stephensi*, *Anopheles culicifacies* s.l. and *Anopheles fluviatilis* s.l. A databank was created which included all published data about *Anopheles* species of Iran from 1961 to 2015. The suitable environmental niches for the three above mentioned *Anopheles* species were predicted using maximum entropy model (MaxEnt). AUC (area under Roc curve) values were 0.943, 0.974 and 0.956 for *An. stephensi*, *An. culicifacies* s.l. and *An. fluviatilis* s.l respectively, which are considered as high potential power of model in the prediction of species niches. The biggest bioclimatic contributor for *An. stephensi* and *An. fluviatilis* s.l. was bio 15 (precipitation seasonality), 25.5% and 36.1% respectively, followed by bio 1 (annual mean temperature), 20.8% for *An. stephensi* and bio 4 (temperature seasonality) with 49.4% contribution for *An. culicifacies* s.l. This is the first step in the mapping of the country's malaria vectors. Hence, future weather situation can change the dispersal maps of *Anopheles*. Iran is under elimination phase of malaria, so that such spatio-temporal studies are essential and could provide guideline for decision makers for IVM strategies in problematic areas.

1. Introduction

Malaria, as an old serious disease, is still a public health problem in tropical and subtropical regions. About 3.2 billion people are at risk of malaria. There was an estimation of 214 million new cases and 438 deaths in 2015 (WHO, 2015). It is still a potential danger in many countries of Africa, Latin America and Asia, including Iran. Malaria is one of the most important vector-borne diseases. WHO and the World Meteorological Organization have classified malaria as the most weather-sensitive disease (Houghton, 1997; WMO and WHO, 2011). *Anopheles* mosquitoes are known as vectors of malaria, and are one of the best examples that are influenced by climate change. They can transmit different species of *Plasmodium* as well as other pathogens (Afrane et al., 2012). Global warming has an effect on human health in two ways: first, it has a direct effect like heat shock, and the other indirect effect, such as transmission of infectious diseases (IPCC, 2007; Bezirtzoglu et al., 2011). There are many infectious diseases that are influenced by environmental changes, but the most sensitive, mosquito-borne diseases. These groups are the largest health problem in global warming (Bezirtzoglu et al., 2011). Arthropods are cold-blooded animals so that small change in the environmental temperature can alter their life cycle and affect their biological and physiological features such

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as geographical distribution, behaviour, growth, reproduction, biting rates, etc. (Patz et al., 2008; Bezirtzoglu et al., 2011; Hiwat and Bretas, 2011). The mean temperature of the earth is rising by 2.6–4.8 °C by 2100. This means that there will be an increase in the insect's bite, parasite survival and parasite development rate, and a decrease in the gonotrophic cycle and larvae growth period (Blanford et al., 2013). This will lead to the spread of *Anopheles* to higher altitudes (Siraj et al., 2014).

Malaria is an endemic disease in the Southern and Southeastern provinces of Iran: Sistan and Baluchistan, Hormozgan and the Southern parts of Kerman (Hanafi-Bojd et al., 2012). Over the last 25 years, there has been a dramatic reduction of the malaria burden in I.R. Iran. According to the report of the Iranian Ministry of Health and Medical Education, the annual malaria cases in I. R. Iran have decreased from 100,000 in 1991–799 in 2015. The latest number of autochthonous cases in the whole country is 42 including 23 local malaria cases, 7 relapsed cases, 12 imported from the other districts by end of July 2016 (Ministry of Health, 2016). In 2010, I.R. Iran set time-bound elimination objectives for its malaria program, therefore, Iran has been classified to be in the elimination phase by WHO (WHO, 2011; Hemami et al., 2013). Locally transmitted cases are now concentrated in the south-eastern part of the country, which are affected by extensive population movement across the border with Pakistan, where malaria control faces serious difficulties. There has been excellent progress since, but the continued risk of importation of malaria cases from Pakistan poses a huge challenge, politically, socially, operationally and technically, to malaria elimination in Iran.

There are five malaria vectors in the South and Southeast of Iran: *An. stephensi, An. dthali*, *An. culicifacies* s.l ., *An. fluviatilis* s.l ., and *An. superpictus* s.l. while *An. pulcherrimus* has been described as a suspected vector (Zaim, 1993; Hanafi-Bojd et al., 2011; Hemami et al., 2013). Among these mosquitoes, 3 species seem to have more important role in the transmission of malaria: *An. culicifacies* s.l., *An. fluviatilis* s.l. and *An. stephensi*.

Anopheles culicifacies Giles s.l. which is mainly recorded from southeastern parts of Iran has introduced as the main malaria vector in some parts of Sistan and Baluchistan Province. This species has two siblings A and B in Iran. In its distribution range, *An. culicifacies* s.l. has two peaks of activity in April–May and August–November. Considering climate, this *Anopheles* is mainly reported from moderate semi-arid and southern part of absolute arid climates in Iran. Previous studies in the area suggested high proportion of exophagic behavior with a human blood index of 1.18–20% and sporozite rate of 1–4.7% (Hanafi-Bojd et al., 2011).

Anopheles fluviatilis James s.l. is a complex species includes T and U forms (Naddaf et al., 2012). The distribution of this *Anopheles* is wider than *An. culicifacies* s.l. from southwest to southeast of Iran. It is considered as a secondary vector for malaria with sporozoite rate of 1.4–11% in southern parts of the country. Because its exophilic and exophagic habits they escape from the indoor residual spraying and so can maintain the malaria transmission cycle in the area in absence of strong endophilic vectors like *An. stephensi*. Due to preference of *An. fluvitalitis* s.l. for breeding in slow flowing waters, especially in higher altitudes and mountainous areas, it has one peak of activity in August in highlands, while in lowlands it has lower density but two peaks in April-June and September-December (Hanafi-Bojd et al., 2011).

Anopheles stephensi Liston is the main vector of malaria in coastal areas of southern Iran, with three phenotypes: mysorensis, typical and intermediate (Oshaghi et al., 2006; Vatandoost et al., 2006; Hanafi-Bojd et al., 2011; Yeryan et al., 2016). Although this species is mainly distributed in lowlands, but there are reports from southern slopes of Zagros chain with an altitude of more than 1800 m (Amani et al., 2014). Previous studies in coastal areas, reported this species is active during the year with two peaks of activity in April-May and September-October, although in highlands higher densities occur in warmer months (Vatandoost et al., 2006; Hanafi-Bojd et al., 2012; Yeryan et al., 2016). Although soprozoite rate of this species reported from 0.2 to 1.8%, comparing other species it has stronger vectorial capacity because higher density, endophagic and endophilic behavior.

The aim of the regional malaria control strategic plan is to reduce local malaria transmission by some vector control measures such as indoor residual spraying, the use of larvicides and the distribution of insecticide-treated mosquito nets (ITN) for the elimination of malaria by 2025 in Iran (Hemami et al., 2013). In this way, forecasting the geographical distribution of malaria vectors is very important for malaria control planning. Noticeable advances have occurred in malaria control programs in the past decades, but changes in environmental conditions, population dynamic and land use are important threats (Tadei et al., 1998; Vittor et al., 2006).

Spatiotemporal modeling of vectors is fast growing. This method, in addition to predicting vector and disease distribution, can improve control measures, and can be used to compare the past and present control systems (Fuller et al., 2012a,b; Drake and Beier, 2014). Ecological niche modeling has been considered in recent years for predicting the most favorable areas for different species, using occurrence records and environmental data (Foley et al., 2008; Sinka et al., 2010; Fuller et al., 2012a; Hanafi-Bojd et al., 2015a,b; Gholamrezaei et al., 2016). Development of a database for malaria vectors and entomological surveillance is critical in the prediction of malaria transmission potential, especially during elimination phase.

This study was aimed to collect all faunistic studies on the main malaria vectors in the endemic areas of Iran, to establish the first spatial database and to predict best ecological niches for these *Anopheles* mosquitoes.

2. Materials and methods

2.1. Study area

Iran encompasses an area of 1,648,000 square kilometres in the Middle East, and is located between latitudes of 25° 3′ to 39° 47′ North and longitudes of 44° 5′ to 63° 18′ East in west Asia, between the Caspian sea in the north and the Persian Gulf and Oman sea in the south. It is surrounded by seven countries, Armenia, Azerbaijan and Turkmenistan in north, Afghanistan and Pakistan in east and at last Turkey and Iraq in west (Fig. 1). The country is situated in the Palearctic zone, but a small area in the south east corner is in the Oriental region. This country experiences a variable climate, from cold weather in northwest to hot and dry in southern parts, and is one of the most unique countries in terms of weather. The difference between the hottest and coldest point sometimes reaches more than 50°C, but, overall, has a temperate and dry climate. The mean precipitation is 250 mm annually, but in highlands and northern coast of the Caspian Sea, the rainfall is measured nearly 500–1000 mm in some western parts (Meteorological Organization of Iran). Suitable environmental conditions such as temperature and humidity in the south and south east regions have provided favourable conditions for malaria disease transmission in Sistan and Baluchistan, Hormozgan and south of Kerman Provinces which lie in subtropical climate.

2.2. Species or occurrence data

Geographical distribution data of Iranian *Anopheles* were obtained from more than 250 valid faunistic references about *Anopheles* from 1961 to 2015. This databank included more than 83 graduates and PhD thesis from Tehran University of Medical