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MODELLING POTENTIAL SNAKEBITE RISKS OF THE ENDEMIC IRANIAN VENOMOUS SNAKE *MACROVIPERA RAZII* (SERPENTES: VIPERIDAE) UNDER CLIMATE CHANGE

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ENDEMIC REPTILES
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IRAN

ABSTRACT. – The potential distribution of one the most venomous snake species of Iran, the endemic *Macrovipera razii*, has been studied. A total of 54 occurrence records with four informative environmental variables, including temperature seasonality (bio4), annual precipitation (bio12), precipitation seasonality (bio15), and precipitation of driest quarter (bio17) for present and future periods were used for identifying suitable habitat. Annual precipitation (bio12) was the most important driving factor with 48 % of permutation importance, followed by precipitation seasonality (bio15) with 42.7 % of contribution to the modeling. According to our results and literature, the most suitable habitats of the species are in highland and mountainous regions. Western and southwestern regions of Iran are highly suitable areas for *M. razii* according to current conditions, which are highly compatible with its known distribution, with the exception of the predicted suitability in a small patchy region of northeastern Iran where another related taxon, *Macrovipera lebetina* subsp. *cernovi*, is present. Future predictions reveal a similar potential distribution. Further research on *M. razii* is crucial and should encompass various aspects such as the analysis of venom components, field studies, and comprehensive molecular investigations. These efforts are necessary to determine the taxonomic status of *M. razii*, understand its distribution patterns, and develop effective anti-venom treatments.

INTRODUCTION

Venomous snake populations are declining and 31 species are listed by the International Union for Conservation of Nature (IUCN) as vulnerable, endangered or critically endangered (IUCN, 2020). Hence, conservation of snakes, especially venomous snakes, is a big challenge (Maritz *et al.* 2016). The World Health Organization (WHO) reported an average of 2,500,000 snakebites envenoming world-wide each year, especially in Southern and Southeastern Asia, Latin America and Africa, which are all with high numbers of venomous reptiles (Kasturiratne *et al.* 2008, Cruz *et al.* 2009, Bickford *et al.* 2010, Nori *et al.* 2014, Ochoa-Ochoa *et al.* 2014, Meng *et al.* 2016). During 2002-2011, 53,787 snake bite victims were acknowledged to the health centers and hospitals throughout Iran. The annual incidence of snake bites is from 4.5 to 9.1 for each 100,000 people. A total of 6,231 snake bite cases were reported in 2006 and 4,696 in 2010, considered as the highest and lowest incidents of snakebites, respectively. The highest mortality occurred in 2005 with 12 death cases and the lowest rate in 2007 with 3 cases (Dehghani *et al.* 2014).

The most important species responsible for most snakebite incidents in Iran, are species belonging to the Viperidae family, including *Macrovipera lebetina*, *Echis carinatus* subsp *sochureki*, *Pseudocerastes persicus*, and *Montivipera raddei* and to the Elapidae family, especially *Naja* (*naja*) *oxiana* (Dehghani *et al.* 2014). Despite the global high frequency of snakebite in terms of morbidity and mortality, the issue has not received adequate attention from national and international health agencies and foundations, research agendas, and pharmaceutical companies (Williams *et al.* 2010), and it is now considered as a ‘neglected tropical disease’ by the WHO (2018). However, snakebite envenomation is a crucial public health challenge in many regions of the world, especially in regions with high rates of snakebite, such as southern and southeastern Asia, sub-saharan Africa, Central America, and South America (Gutiérrez *et al.* 2010). All knowledge about the distribution of venomous snakes needs to be localized in order to estimate where risks of accidents are the highest (Harrison *et al.* 2003).

Using species distribution modelling (SDMs) is a common approach to predict current and future distribution maps for surveying snakebite incidence risks (Nori *et al.* 2014, Yañez-Arenas *et al.* 2014, 2015, Needleman *et al.* 2018). Increasing knowledge of spatial patterns in snake distribution and predicting regions at high risk of snakebite is critical for planning and managing snakebite envenomation issues (Pintor *et al.* 2021).

Climate change will pose significant challenges to biodiversity conservation in the future (Li *et al.* 2020). Future climate change can lead to shifts in the distribution and abundance of species (Wang *et al.* 2018), extinction of species populations (Fois *et al.* 2016), range shifts (Erfanian *et al.* 2021, Habibzadeh *et al.* 2021), phenological changes (Anenkhonov 2009, Cuena-Lombraña *et al.* 2018) and physiological trait changes (Fois *et al.* 2018a, b, Habibzadeh & Ludwig 2019, Kaky & Gilbert 2019). Ectothermic animals, such as reptiles, are further threatened by climate change owing to their sensitivity to changes in the thermal landscape and low dispersal ability (Sinervo *et al.* 2010). Studying the effects of future climate change on distribution of species is one of the fundamentals to manage informative activities for conservation of biodiversity (Kaky & Gilbert 2017, 2019, Fathinia *et al.* 2020, Hosseinzadeh *et al.* 2020). Hence, species distribution modelling (SDMs) can predict potential current, past, or future species ranges and shifts (Hijmans & Graham 2006).

In this study, we reported comprehensive occurrence localities of *M. razii*, a venomous snake endemic to Iran. According to presence records, we identified important environmental drivers to build its potential distribution under current and future climatic habitats. In addition, we provide information and discuss about the risk of snakebite in Iran.

MATERIALS AND METHODS

Study species: The genus *Macrovipera* mainly occurs in Asia, where it lives in semi-deserts and steppe habitats of Jordan, Syria, Turkey, Iraq, Iran, Azerbaijan, Turkmenistan, Uzbekistan, Tadzhikistan, Kyrgyzstan and Afghanistan (Joger 1984, Bruno 1985). Three taxa of two species and three subspecies of the genus *Macrovipera* have been reported from Iran: *Macrovipera lebetina* subsp. *obtusa* (Dwigubsky, 1832) in western and northwestern Iran and Alborz Mountains, *M. lebetina* subsp. *cernovi* (Chikin & Szczerbak 1992) in northeastern parts of Iran and *Macrovipera razii* subsp. *razii* (Oraie *et al.* 2018) central and southern parts of Zagros Mountains (Moradi *et al.* 2014; Oraie *et al.* 2018; Uetz *et al.* 2022).

Macrovipera razii is endemic to Iran and the type locality is located 105 km on the road from Jiroft to Bam near Bab-Gorgi village, Kerman Province at an elevation of 3150 m. Referring to the terrestrial ecoregions defined by Olson *et al.* (2001), *M. razii* is present in Central Persian desert basins, South Iran Nubo-Sindian desert and semi-desert, Kuh Rud and Eastern Iran Montane woodlands and Zagros Mountains forest steppe. It differs from *M. lebetina* by distinctive morphological characters including elongated anterior chin-shields more than three times longer than the posterior ones, and more ventral scales between 172-175 versus 160-170 in other Iranian *Macrovipera* (Oraie *et al.* 2018, Fig. 1). Interestingly, *M. razii* and *M. lebetina cernovi* are similar in both possessing one large supraocular scale, which is absent in *M. lebetina obtusa*. The genetic distance between populations of *M. razii* and *M. lebetina cernovi* is greater compared to *M. lebetina obtusa*. (Oraie *et al.* 2018, Freitas *et al.* 2020).

Species distribution modelling: A total of 54 occurrence records of *M. razii* were compiled from personal field observations and literature sources (Frynta *et al.* 1997, Sindaco *et al.* 2013, Kazemi *et al.* 2015, 2021, Oraie *et al.* 2018, Oraie 2020, Uetz *et al.* 2022) and then used for species distribution modelling in Bushehr, Chaharmahal & Bakhtiari, Fars, Isfahan, Kerman, Khuzestan, Kohgilouyeh & Boyer-Ahmad, Lorestan, Markazi, Qom and Yazd Provinces.

Through species occurrence data and environmental information, we generated environmental niche models that were used to predict the location of particular areas where environmental conditions are favorable for the presence of the study species. Maximum Entropy modeling (MaxEnt) is a very powerful presence/pseudo-absence algorithm. Many authors have suggested that it is one of the most efficient approaches for predicting species' potential distributions (Hijmans *et al.* 2005, Phillips *et al.* 2006, Elith *et al.* 2011, Fois *et al.* 2018a). Herein, MaxEnt was used with default settings with ten replicates, a technique that has been proven to achieve high predictive accuracy (Fois *et al.* 2018a). Convergence threshold and maximum number of iterations were done by default (0.00001 and 500, respectively).

The presence records have been randomly divided into 70 % for model calibration and 30 % for evaluation. The 'area under the receiver-operating characteristic curve' (AUC) was used for model evaluation, which measures the ability of a model to distinguish between sites where a species is 'present' versus 'absent' (Phillips *et al.* 2006). According to Manel *et al.* (2001), models with AUC = 0.5 measure a performance equivalent to random; AUC > 0.7 measures useful performance, AUC > 0.8 mentions good performance, and AUC ≥ 0.9 measures excellent performance. The difference between training and testing AUC (AUC_{DIFF}) was used to measure the degree of model overfitting,

Fig. 1. – Image of *Macrovipera razii* in its habitat. Photographed by S M Kazemi.

and the receiver operating characteristic (ROC) curve was used to verify the prediction accuracy of the potential species distribution (Elith *et al*. 2011).

In total, 19 variables related to bioclimatic seasonality and annual trends of temperature and precipitation were downloaded from the WorldClim database (http://www.worldclim.org; Hijmans *et al*. 2005) for the present climate conditions (1970-2000). For future periods, the environmental factors have been downloaded for the years 2070, average for 2061-2080. The models were projected for both 2.6 and 8.5 representative concentration pathway (RCP) emission scenarios. For future projections, three general circulation models (CCSM4, MIROC5 and GISSE2-R) were used (Fois *et al*. 2018b, Farashi & Erfani 2018, Hosseinzadeh *et al*. 2020). We chose the RCP 8.5 because it showed distribution patterns of species corresponding to intensive scenarios with rising temperature approximately to 2.4-4.4° C (Newth & Gunasekera 2018). All environmental layers have been extracted at a spatial resolution of 30 arc seconds (grid cells of ~0.0083° – approximately 1 km). The mentioned layers have been clipped for Iran territory by ARCMAP 10.4.1. To achieve the final map for RCP 8.5, we averaged the predictions from the three GCM using DIVA-GIS (Hosseinzadeh *et al*. 2020, Valtueña *et al*. 2020, Scherrer *et al*. 2021).

Following Yousefi *et al*. (2020), four out of 19 environmental variables were chosen and used in this study including temperature seasonality (bio4), annual precipitation (bio12), precipitation seasonality (bio15), and precipitation of driest quarter (bio17).

RESULTS

Model performance for current climate conditions was high with average AUC = 0.854 ± 0.065. $\mathrm{AUC}_{\mathrm{DIFF}}$ was 0.053. Both present and future model predictions showed western and southwestern regions of Iran as highly suitable areas according to informative environmental variables and their geographic position for *M. razii* (Fig. 2). In addition, the model also outscored northern and northeastern regions of Iran as suitable for the species (Fig. 3). Highly suitable habitats of western and southwestern Iran coincide with the already known distribution range of *M. razii*. The northeastern Iran showed similar climatic characteristics but another species*, M. lebetina cernovi,* is present.

Among the environmental variables, annual precipitation (bio12) was the most important driving factor with 53 % contribution, followed by precipitation seasonality (bio15) with 36.2 % contribution. In terms of permutation importance, annual precipitation (bio12) and precipitation seasonality (bio15) scored 48 % and 42.7 %, respectively (Table I). Significant differences between current and future predictions were not found. In addition to the ecological implications, the same results provide information on the higher risks of snakebite where the species' suitability is high and how this pattern might change in the future.

DISCUSSION

Our finding shows that western and southwestern regions of Iran are highly suitable areas for *M. razii* according to current and future conditions. This is in line

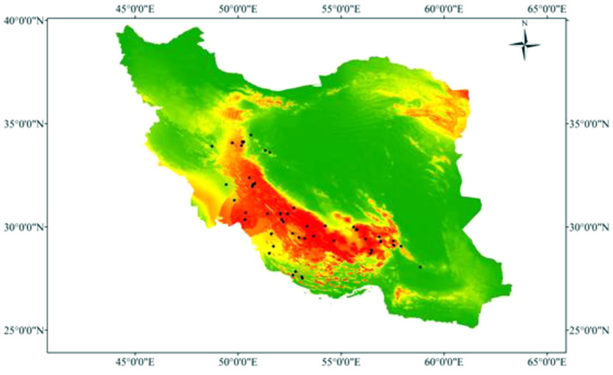

Fig. 2. – Potential distribution of *Macrovipera razii* resulting from the average MaxEnt model. Black dots showed occurrence records of *M. razii*. Red to green show high to low habitat suitability, with more intense colors indicating more extreme values.

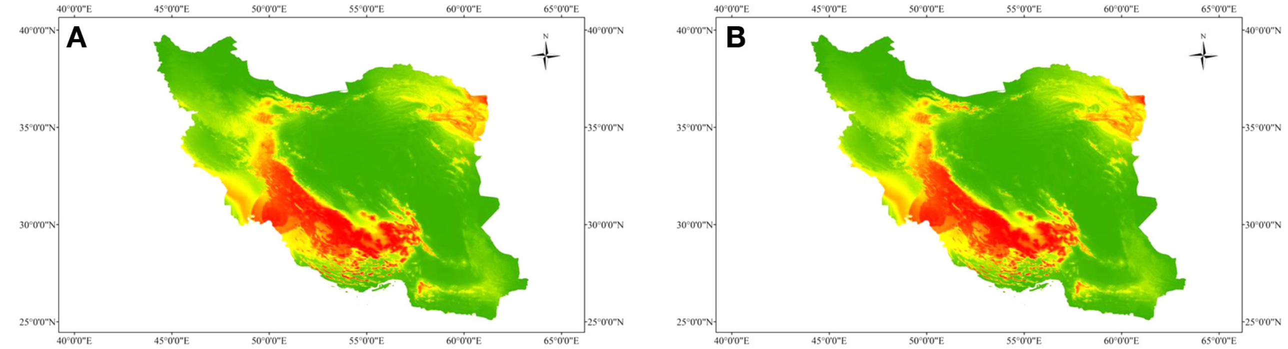

Fig. 3. – Future projection model pattern of *Macrovipera razii* under two scenarios as (**A**) 2.6 Representative Concentration Pathway, (**B**) 8.5 Representative Concentration Pathway. Figures show the average of results according to four Global Circulation Models (CCSM4, HadGEM2-ES ,MIROC5, GISSE2-R).

Table I. – Contribution percentages of important variables included in the MaxEnt distribution model for *Macrovipera razii*.

Variable	Percent contribution	Permutation importance
bio12	53	48
bio15	36.2	42.7
bio17	10	6.8
bio4	0.8	2.5

with the known distribution pattern of the species and corresponds to the Zagros Mountains. However, the model indicated that the northern and northeastern regions of Iran have suitable habitat conditions for *M. razii* based on current climate, even though no records of *M. razii* have been reported in these areas. Northern and northeastern Iran and in particular Kopet-Dagh Mountains host *Macrovipera lebetina* subsp. *cernovi*. According to molecular studies, *M. lebetina* is closely related to *M. razii* (Oraie *et al*. 2018, Oraie 2020). At least two geographic barriers influence the distribution disjunction of these species. Zagros Mountains are also crucial biological barriers for fauna and flora, separating western from central and eastern regions of Iran. Accordingly, Oraie *et al*. (2018) suggested that *M. razii* genetically isolated from the other studied populations of *M. lebetina* along with the rise of the Zagros Mountains in the late Miocene some 12-10 Mya. Ecological and geographical divergence driven by Zagros Mountains uplift was reported for other taxa, such as species and evolutionary significant units of the genera *Montivipera* (Ahmadi *et al*. 2021) and *Testudo* (Turkozan *et al*. 2021) and several other vertebrates (Yousefi *et al*. 2022, and references therein).

Species distribution models (SDMs) can be utilized to generate snakebite risk maps by assessing the habitat suitability of venomous snakes. This approach is particularly valuable in regions with high snakebite risk and where data on snake populations are limited. For instance, SDMs may become important tools in public health research for some venomous species that may expand their distribution ranges under climate change and, accordingly, change their envenoming risk (Yousefi *et al*. 2020, Kazemi *et al*. 2023). According to many studies, future distribution of the species should retreat to northern latitudes and higher elevations (Ahmadi *et al*. 2019, Hosseinzadeh *et al*. 2020, Yousefi *et al*. 2020) but this study did not show significant differences between current and future species models.

Based on Oraie *et al*. (2018), the habitat of *M.razii* is different from altitudes above 3000 m at the type locality in Kerman Province to about 1500 m near Lake Bakhtegan in Fars Province. The vegetation of type locality is relatively dense including *Orchis*, *Zygophyllum* and *Astragalus* spp. The study area exhibits a predominantly cold mountain climate characterized by long and cold winters. However, it is noteworthy that *M. razii* was also observed in a significantly distinct habitat characterized by warmer and drier conditions, particularly in the vicinity of Lake Bakhtegan. In addition, Harsh mountain habitats are another type of habitat for that species.

According to our findings, annual precipitation (bio12) and precipitation seasonality (bio15) were the most important driving factors. This is in line with several studies that showed that precipitation-related variables were the most influential factors that affect the distribution of many taxa in the mountainous areas of the Iranian-Turanian region, such as *N. oxiana* (Yousefi *et al*. 2020), *Testudo graeca* (Turkozan *et al*. 2021), but also mammals (Kaky *et al*. 2023), and plants (Behroozian *et al*. 2020, Karami *et al*. 2022).

Despite the WHO reports (2018) on the high medical importance of *M. lebetina* in Iran, Iraq, Lebanon, Syrian and Turkey, no antibodies based on *M. razii* venom are in the polyvalent antivenom of the Razi Vaccine & Serum Research Institute, which is the only center producing antivenoms in Iran. Bites from *M. lebetina obtusa* usually cause life-threatening systemic hemodynamic disturbances, reduced functionality of the kidneys, and other serious symptoms including hypotension shock, edema, and tissue necrosis at the bite site (Kazemi *et al*. 2021). In Iran, *Echis* and *Macrovipera* genera comprise wide distribution and the highest number and severity of envenomation by snakes (Dadpour *et al*. 2012, Dehghani *et al*. 2014, Kazemi *et al*. 2021). The antibodies against venom of the following species are already present in the antivenom: *Naja* (*naja*) *oxiana, Gloydius caucasicus, Echis carinatus* subsp. *sochureki, M. lebetina, Montivipera raddei* and *Pseudocerastes persicus*; we believe that antibodies against the *M. razii* venom should also be included.

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