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HEALTH SCIENCES

The challenge in detecting risk areas of snakebite when case rates are low: the case of Amazonian coral snakes

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Abstract: Identifying risk areas for envenomation by animals is relevant for public health, such as strategic distribution of antivenoms. Coral snakes are highly diverse in the Amazon, inhabit natural and human-modified environments, and the outcome of the cases tends to be serious and potentially lethal due to their neurotoxic venom. By integrating species' geographical records and environmental variables, we used species distribution modeling to predict the distribution of coral snake species in the Brazilian Amazonia. We analyzed the relationship between the predicted distribution of coral snake species, along with envenomation data in the region, to propose actions to reduce the number of cases and to provide tools for a better policy of public health. We conclude that the entire Amazon shows high environmental suitability for coral snakes, and such suitability explains little about the incidence of cases. This is probably due to the low human density in the Amazon and to coral snake traits such as secretive habits and non-agressive behavior. Differently from other venomous snakes, the scenario regarding coral snakebites precludes the detection of prominent geographical areas of concern and demands a broad and equitable availability of health centers throughout Amazonia and along other areas of occurrence of the genus *Micrurus*.

Key words: Elapidae, Human Health, Neglected Tropical Diseases, *Micrurus*, Species Distribution Modeling.

INTRODUCTION

Snakebite envenomation (hereafter SBE) is considered a non-infectious neglected tropical disease that requires urgent funding for research and public policy actions integrating ecological, epidemiological, and clinical aspects in wider geographical contexts (Chippaux 2017a, Martín et al. 2022). In Brazil, 430 species of snakes are recorded, of which 70 species (16.27%) are venomous (families Viperidae and Elapidae) (Melgarejo 2009, Costa et al. 2021). Although they represent the minority of species, venomous snakes were responsible for an annual average of ~30,000 snakebites/year. Between 2010 and 2020, the Brazilian Amazonia region concentrated 42.6% of snakebites reported in Brazil (SINAN 2022), with 0.6% of case fatality between 2000 and 2016 (Fan & Monteiro 2018). Given that most of the human displacement in the immense Amazonian territory is done by boats, and the fact that the closest health centers can be hours or days away, a strategic distribution of health centers containing antivenoms for the cases that occur in this region is vital to reduce the chances of human mortality.

Snake antivenoms are considered the only effective treatment against SBE (WHO 2018).

In many parts of the world, antivenoms are expensive, scarce, and poorly distributed, and countries with difficulties in purchasing and strategically distributing them have the highest mortality (Gutiérrez et al. 2006, Harrison et al. 2009). One of the challenges in addressing the lack of antivenoms involves specifying their requirements at an operational, local level, through the collection of epidemiological data (Chippaux 2017a). In the Americas, for instance, the reporting to SBE in many countries became mandatory in the last decade which increased the epidemiological data available (Chippaux 2017b). In Brazil, a system for providing antivenom based on epidemiological information was established, according to an estimated demand for each state (CNCZAP 1991, Gutiérrez et al. 2009, Fan & Monteiro 2018). With the advent of this system, there was a considerable decrease in the annual mortality rate resulting from snakebites (Cardoso & Wen 2009).

One of the richest groups of venomous snakes in the country is represented by the coral snakes (family Elapidae, genera *Leptomicrurus* and *Micrurus*), represented by 38 species widely distributed in the national territory and occurring in all kinds of natural (and sometimes even disturbed) landscapes (Silva Jr. et al. 2021, Costa et al. 2021). In Amazonia, they occur in forested, open, and disturbed areas and at least two species (*Micrurus lemniscatus* and *M. surinamensis*) are found in urban environments (e.g. Martins & Oliveira 1998, Rodrigues et al. 2016, Almeida-Correa et al. 2020). Only 13.3% of the Brazilian population resides in the Amazonia, however, the region concentrated 42.6% of the snakebites reported for the country between 2010 and 2020 (SINAN 2022). Although coral snakes cause less than 1% of snakebite cases recorded for the Amazonia, the outcome of the clinical condition tends to be serious: several of the cases are considered severe and some of them evolve with early neuroparalytic manifestations (Bisneto et al. 2020a, b). In general, symptoms presented by victims bitten by coral snakes in the region include: erythema, pain, paresthesia, numbness, palpebral ptosis, salivation, blurred vision, dysarthria, dysphagia, diplopia, dyspnea, and muscular weakness (Bisneto et al. 2020a, b).

Brazilian Amazonia has a long history of land use, especially in the southern/eastern borders (Margulis 2004), and deforestation in the area has been associated with an increased risk of snakebites (Ferreira et al. 2020). However, envenomation by coral snakes in this region is rare and sparse over long intervals of time, making it difficult to detect epidemiological patterns (Bisneto et al. 2020a). Normally, snakebite risk assessments are based on the relationship between the abundance and species richness of venomous snakes related to human aspects, such as population density (Ochoa et al. 2021, Glaudas 2021, Martín et al. 2022). In Latin America, most of the snakes involved in bites are viperids (genera *Crotalus* and *Bothrops*), and coral snakes are commonly left out from epidemiological analyses (Yañez-Arenas et al. 2014, 2018). It worths mentioning that in Amazonia, there are numerous poorly-accessible areas, research centers are concentrated in few cities, that along with the secretive (fossorial) life habits of *Micrurus* result in a lack of detailed data on species' ranges (Wallacean shortfall sensu Whittaker et al. 2005). *Micrurus* represents a clear example as the knowledge about species distributions is very incomplete and how it could impact public heath (Terribile et al. 2018, Nogueira et al. 2019).

Information about geographical distribution (based on point occurrence or predicted distribution) of venomous snakes has being recognized as crucial in public health planning allowing estimating areas of risk of accidents that should be prioritized for health centers, but also for collecting venom for antivenom production from the entire range of the species (see Nori et al. 2013). It follows the recently released Ecohealth perspective that understands that areas of risk of snakebites can change under climate change scenarios (Gutiérrez 2020). In recent years, Species Distribution Modeling (hereafter SDM) methods have been used to predict geographic distribution areas for species (Elith & Leathwick 2009, Peterson et al. 2011, Araújo et al. 2022). In the context of venomous snakes and SBE, this method can be used to predict the distribution of species of medical importance, help planning an adequate antivenom distribution policy, including production logistics, prevention policies, and monitoring of risk areas (Yañez-Arenas et al. 2018, Citeli et al. 2020). The use of ecological data is especially relevant when there is a lack of information on the species distribution (i.e., fossorial species), allowing the prediction of species distribution and thus identifying high-risk areas of snakes envenoming. The goal of this study is, by integrating updated species' geographical records and environmental variables, to use SDM to predict the distribution of medically important coral snake species in the Brazilian Amazonia. We also aimed to analyze these results with data on envenomation in the region, in order to propose actions to reduce the number of envenomations by *Micrurus* and to provide tools for a better policy of public health.

MATERIALS AND METHODS

Study Area

The Amazonian biome (Figure 1) contains the largest tropical forest in the world with ca. 6 million km^2, and almost 60% of its territory lies within the Brazilian border (Coca-Castro et al. 2013). It is characterized by its forest integrity where vegetation is composed mostly of dense ombrophilous forest (IBGE 2012). The local climate is hot and wet. The monthly thermal amplitude is low, ranging 2° C along the year. The average rainfall is 2300 mm per year, showing a heterogeneous temporal and spatial distribution, but in most of the region the rainy season occurs between November and March and the dry season between May and September (Figueroa & Nobre 1990, Fisch et al. 1998, INMET 2022). Currently, 47.2% of the area is covered by indigenous territory or protected natural areas (RAISG 2020) (Figure 1a).

Amazonia covers totally or partially municipalities in nine Brazilian states: Acre, Amapá, Amazonas, Maranhão, Mato Grosso, Rondônia, Roraima, Pará, and Tocantins (SUDAM 2007, IBGE 2020a). The estimated population is 22.39 million people in 2015 (IBGE 2013), of which about a fifth are concentrated within the five largest cities, with a density of 5.60 inhabitants/km^2 (IBGE 2020b). It is also evident that there is a high concentration of indigenous people due to the abundance of their territories (Figure 1d), which comprise 2,376,140 km^2, equivalent to 27.5% of the entire biome (RAISG 2020). Since 1970, the main drive of land-use in the region has been the expansion of the area devoted to planted pasture (Margulis 2004) (Figure 1b). Other pressures threatening the region include crops, mines, hydroelectric dams and the presence of roads (Margulis 2004, MMA et al. 2007, Lees et al. 2016, Ferrante & Fearnside 2020, Ferrante et al. 2021).

Target species and occurrence data

It is known that more than 30 species of two genera (*Micrurus* and *Leptomicrurus*) of coral snakes are found in Brazilian Amazonia (Costa et al. 2021, Silva Jr. et al. 2021). However, in Brazil, only those species of the genus *Micrurus* are known to have caused envenomation in humans

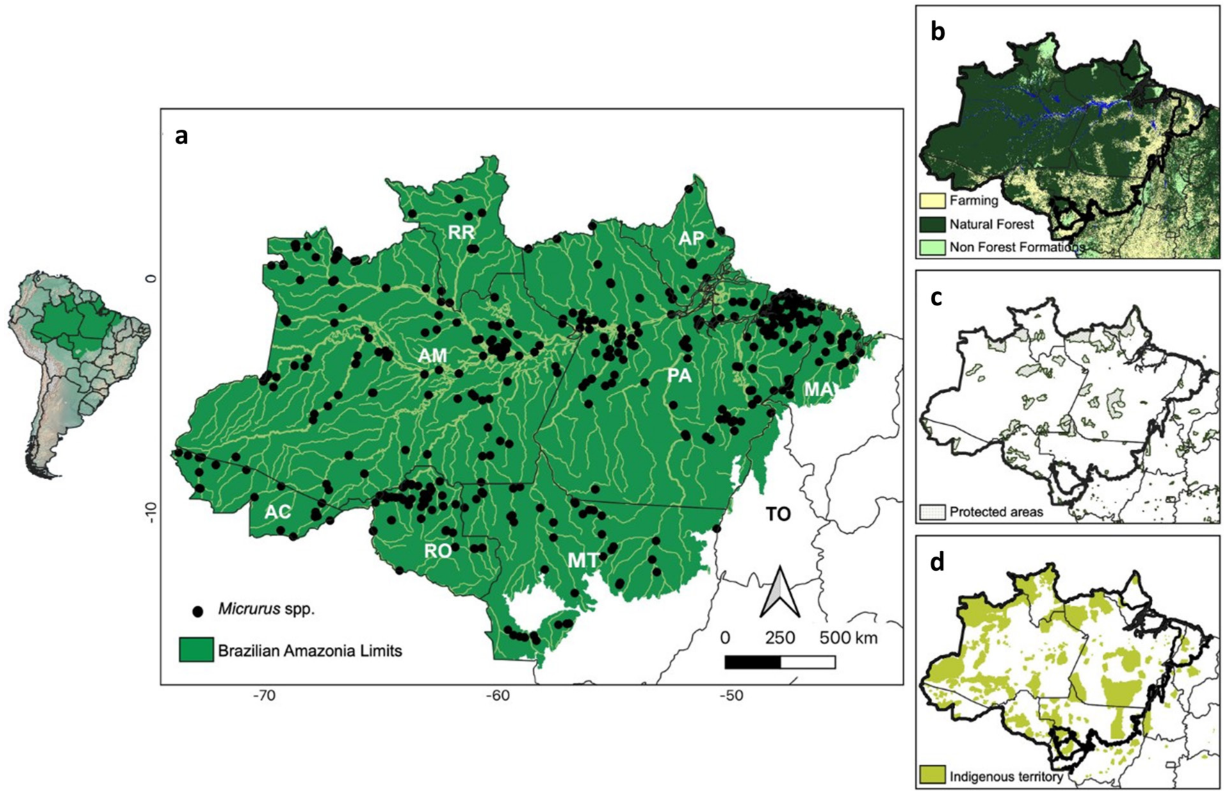

Figure 1. Coral snakes in Amazonia. (a) Limits of the Brazilian Amazonia (merged from IBGE 2019 and Eva & Huber 2005), showing the records for the selected species of coral snake (from Nogueira et al., 2019). (b) Natural habitat remnants, and land cover changes (collection 4, Souza Jr. et al. 2020, MapBiomas 2021). (c) Protected areas (CEM 2021). (d) Indigenous territory (Funai 2019). States abbreviations: AC: Acre; AM: Amazonas; AP: Amapá; MA: Maranhão; MT: Mato Grosso; PA: Pará; RO: Rondônia; RR: Roraima; TO: Tocantins.

(Bisneto et al. 2020b). We considered in our study those species of *Micrurus* with at least one point occurrence inside the limits of the biome (Fig. 1); those species with at least 20 point records distant ~3 km from each other (see details below in section Species distribution modeling); and those with typical forested distribution, i.e., we excluded species from the Cerrado that showed few records inside the study area (e.g. *Micrurus frontalis*).

Although only seven species of *Micrurus* are known to cause envenomations in the Brazilian Amazon (Bisneto et al. 2020b), we decided to include all possible species (see above) because in the Amazon, cases of species not reported in the literature may occur due to notification and communication issues, and we consider it is important to analyze the potential distribution of species of potential medical relevance, even if there are no records of envenomations by them. In addition to possible underreporting, there are no specialists at health centers trained in identifying coral snakes at the species level. Furthermore, as they are rare records, we considered all possible distribution data of *Micrurus* as relevant to map.

We obtained occurrence data of species of coral snakes (genus *Micrurus*) (Supporting Information is available in https://github.com/BisnetoPF/Coralsnake_SDM-Brazilian_Amazonia) from online Supporting Information (Table SII) provided by Nogueira et al. (2019) in their work. These distribution data are based on vouchered specimens examined in natural history museums or obtained from literature records (see Nogueira et al. 2019 for further details). After identifying the species occurring within Amazonia, we expanded the occurrence database of these species beyond the region boundaries using data provided by Nogueira et al. (2019). This approach was used because the better we detail the distribution of species, the better we characterize their climatic niches, thus generating more reliable models (Phillips et al. 2004).

Species distribution modeling

We performed a Species distribution modeling (SDM) (Guisan & Thuiller 2005) to estimate the geographic distribution of *Micrurus* species based on environmental suitable areas for the species Brazilian Amazonia. The SDM uses the association of environmental variables with the occurrence data of a species to map their predicted distribution (Guisan & Thuiller 2005).

We obtained 20 variables (19 bioclimatic and one elevation) from the WorldClim database (see http://www.worldclim.org/ for variable descriptions) at a resolution of 5 arc-min (Fick & Hijmans 2017) (WorldClim version 2.1, https://worldclim.org/data/worldclim21.html), averaged over the 1970-2000 period. To avoid overprediction and low specificity, we cropped the environmental layers to span from latitude -90 to -30 and longitude -50 to 15 (values in decimal degrees); this calibration area corresponds to South America limits and was chosen taking in to count that all target species show a cis-Andean geographical range. To reduce autocorrelation among occurrence data and the potential for overfitting we eliminated one of each pair of records falling within single grid cells (~3 km) using the package 'spThin' (Aiello-Lammens et al. 2015). To avoid problems related to the multicollinearity of the environmental explanatory variables, we calculated the Variance Inflation Factor (VIF) values for variables to each species. All values that were highly correlated (VIF > 5) were removed through a stepwise procedure, using the 'usdm' package (Naimi 2013). In general, eight variables were selected for the species: mean diurnal range (BIO2), isothermality (BIO3), temperature seasonality (BIO4), mean temperature of wettest quarter (BIO8), precipitation of wettest month (BIO13), precipitation seasonality (BIO15), precipitation of warmest quarter (BIO18) and precipitation of coldest quarter (BIO19) (Table SI). The variable most frequently chosen as the most important for each species according to the models was temperature seasonality (BIO4).

We performed species distribution modeling for each *Micrurus* species using nine different algorithms implemented in the 'biomod2' package (Thuiller et al. 2016) in R computational environment (R Core Team 2020) including the following: three regression methods [GAM: general additive model (Hastie & Tibshirani 1990), GLM: general linear model (McCullagh & Nelder 1989), MARS: multivariate adaptive regression splines (Friedman 1991)]; three machine learning methods [GBM: generalized boosting model (Ridgeway 1999), MAXENT: Maximum Entropy (Phillips et al. 2006), RF: random forest (Breiman 2001)], two classification methods [(CTA: classification tree analysis (Breiman 1984), FDA: flexible discriminant analysis (Hastie et al. 1994)], and one envelope model [SRE: Surface Range Envelop (Booth et al. 2014)]. To meet the criteria of having absence (or pseudo-absence) data for most of these models (except SRE), we generated two equal-sized (to the true presence records) sets of random pseudo-absence (PA) points across the model background (500 PA points in each set). The models were calibrated using 70% of randomly selected data. The other 30% of the data were used for intrinsic model evaluation.

Individual model performance was evaluated using two metrics: true skill statistic (TSS) and the area under the curve of receiver operating characteristics (ROC) implemented in the 'biomod2' package. TSS is calculated as "sensitivity + specificity -1" and ranges from -1 to +1, where +1 indicates perfect agreement, a value of 0 implies agreement expected by chance, and a value of less than 0 indicates agreement lower than expected by chance. Models with high predictive accuracy (TSS > 0.8) were used for the projection of snake distribution. We constructed ensemble maps based on the median of two runs of all the selected models in which individual accuracy had TSS value equal to or greater than 0.8.

Mapping suitable areas for coral snakes and testing snakebite risk in Amazonia

To characterize the predicted distribution of coral snakes, we created a generalized map of predicted distribution showing the environmental suitability for the genus. Continuous predictions of ensemble models were transformed into a predicted bivariate map of potential presence versus absence of the species, where habitat suitability was identified by stacking and averaging the projections of all species. The generalized predicted distribution map was made using QGIS version 3.16 (QGIS Development Team 2020).

To analyze the risk of venomous snakebites caused by *Micrurus*, we constructed a spreadsheet for each Brazilian municipality of the biome containing data on the number of SBE, the value of predicted snake distribution, and human population density (Table SII). The data of the SBE in each municipality of Brazilian Amazonia caused by *Micrurus* were gathered from the Brazilian Ministry of Health, through the *Sistema Nacional de Agravos de Notificação* – SINAN (Brazilian Information System of Notifiable Diseases), considering the period between 2010 and 2015 and selecting the type of snakebite by "coral snake". To avoid possible confusion with bites by "false" coral snakes (non-venomous species that mimic *Micrurus*), we excluded from the analysis cases that could not be associated with coral snake envenoming, following the classification of bites from Casais-e-Silva & Brazil (2009) and Bisneto et al. (2020b). The values of predicted snake distribution were collected automatically, on QGIS (QGIS Development Team 2020), from a generalized map of predicted distribution (in raster format) using the centroid of each municipality. The values of population density were obtained from Centro de Dados Socioeconômicos e Aplicações (CIESIN 2021) also using the centroid of each municipality. We obtained human population density, and the annual number and incidence rate (given in cases/100,000 inhabitants) of cases.

We tested which variables were related to incidence of Elapidae snakebites in Amazon. For this, we ran the Generalized Linear Models (GLM) using the binary presence of snakebites in Amazon as the response variable and the interaction between the distribution of Elapidae snakes (i.e., risk) and human population density as predictor variables. The model family (i.e., binomial distribution) was selected after inspecting the distributions of the response variables in the diagnostic plots generated in the DHARMa package (Hartig 2022) in the R environment (R Core Team 2021). Model fit of the GLM model was evaluated visually by checking the normality of the model residuals (QQ-plot and plot of the residuals versus the fitted values) and dispersion test from the DHARMa package (Hartig 2022) (Figure S1). For spatial visualization and better discussion of our results, we also provided a map of healthcare centers with snake antivenom. We used the centroid of each municipality in the area and the list of healthcare centers with snake antivenom provided by Citeli et al. (2018), although this list does not detail the amount of each type of antivenom available used in Brazil (against *Bothrops*, *Crotalus*, *Lachesis* and *Micrurus*).

Ethics statement

This study was evaluated, approved, and authorized by the National Research Ethical Committee through the Plataforma Brasil and Ethical Committee of the *Núcleo de Medicina Tropical* of the *Universidade de Brasília* (approval number 1.652.440/2016).

RESULTS

Distribution of coral snakes in Amazonia

We recorded 23 species of *Micrurus* with at least one record in the limits of the biome. After filtering, fourteen species were selected for the SDM (see Target species and occurrence data), totalizing 3,539 occurrences (Figure 1, Supplementary Material A, Table SI, Figure S3). Our database of occurrences of coral snakes is uneven, with most of the records concentrated around major cities and river channels (Figure 1a). The number of records is also uneven. For example, *M. lemniscatus* has over 1,000 records, and many others have hundreds, while species like *M. diutius*, *M. nattereri* and *M. psyches* have less than 100 records (Table SI). A few of species not used in the analyses are known only from the type specimens (e.g. *M. pacaraimae* and *M. tikuna*) (Silva Jr et al. 2021).

Maps for all the species analyzed are available in Figure S3, Supporting Information. Suitable areas for *Micrurus albicinctus* were concentrated in southwest Brazilian Amazonia, in the Amazonas/Rondônia/Mato Grosso border, but also south of Rondônia and in most of the Amazonas. *Micrurus annellatus* showed suitability in western area, mainly in Acre, but also in western Rondônia and southwestern Amazonas. The most suitable areas for *Micrurus averyi* are located in the northern half of Brazilian Amazonia, mainly in the north of the Amazon river, from western Amazonas, through Roraima to Amapá and eastern Pará to Maranhão. *Micrurus diutius* had greater environmental suitability for the northern half of the region, from the western Amazonas to Maranhão, with a few areas of suitability in western Amazonas. *Micrurus filiformis* showed suitability in most of Amazonia, especially in a central corridor from east to west from Acre to Maranhão, following the Amazon river channel and its main tributaries. The suitability areas for *Micrurus hemprichii* were located in most of the Amazonia, especially most of Amazonas, Acre and Roraima, central and eastern Pará, and in the north of the states of Maranhão, Rondônia, and Mato Grosso.

Micrurus langsdorffi had greater environmental suitability for the northwestern Amazonia, almost solely in Amazonas, but with suitable areas in western Acre, northern Rondônia, and southern Pará. *Micrurus lemniscatus* has a pan Amazonian distribution, with suitable areas being found in almost the entire region, with a few exceptions in Amazonas, Pará, and Mato Grosso. For *Micrurus nattereri*, suitability was concentrated in the known area of occurrence, in the northwest end of the region, with a few patches scattered in the other states, except for Acre. *Micrurus obscurus* showed suitability for the western part of the biome, with many areas without records showing a high probability of occurrence, and a few areas of less probability in Pará and Amapá. *Micrurus paraensis* showed suitability in a diagonal area from Maranhão and eastern Pará to Mato Grosso and Rondônia, with areas in northern Amazonia. Suitable areas for *Micrurus psyches* were in the northern half, mainly in northern Pará, Roraima, and Amapá, but also in areas in eastern and central Amazonas. *Micrurus spixii* showed the largest suitable areas among the species analyzed. Almost all the regions, but especially northern Rondônia and eastern Pará, showed high suitability for the species. *Micrurus surinamensis* also showed a large suitable area in Amazonia, with an exception in central Amazonas.

Mapping suitable areas for coral snakes and testing snakebite risk in Amazonia

The general map of predicted distribution indicated areas of suitability for coral snakes in an extensive area in Brazilian Amazonia (Figure 2a), with a pattern of high suitability toward the east. The highest suitability areas were located in eastern and western Pará, eastern and northwestern Amazonas (with an area in the far west, near the border with Peru and Colombia), northern Maranhão, northern Rondônia (with areas in the south of Amazonas, near the border of both states), and southern Roraima (Figure S2). Areas with medium suitability were found in most of Amazonas, the northern half of Pará, the northern half of Roraima, and good portions of Acre, Amapá, and Mato Grosso. Areas of less suitability were found in southern Maranhão, southern half of Pará, open areas in northern Roraima, Tocantins, and southern Amazonian regions of Rondônia and Mato Grosso (Figure 2a).

Between 2010 and 2015, twenty cases of SBE by coral snakes were reported for the 772 municipalities in the study area for all states,

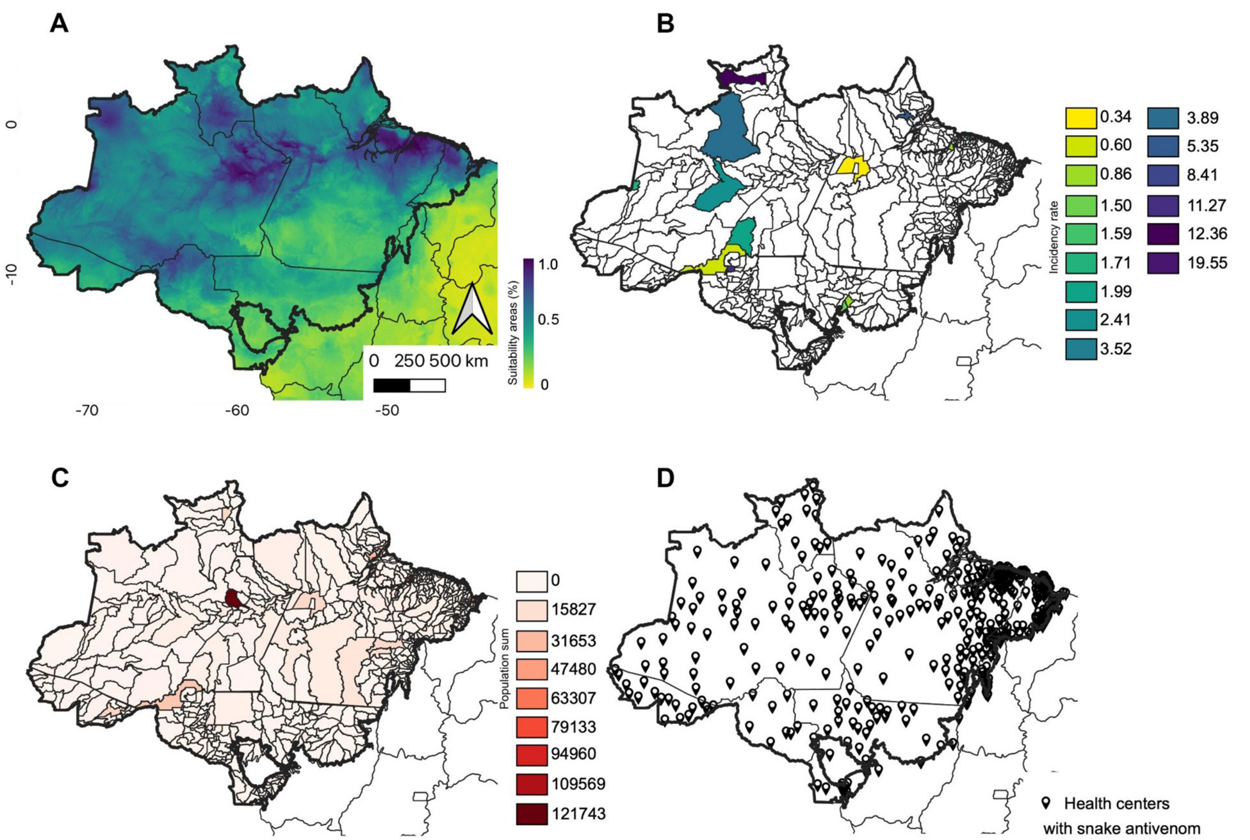

Figure 2. Map of the predicted distribution of coral snakes in Brazilian Amazonia highlighting the most suitable areas for Micrurus (a) incidence rates among municipalities (b), population sum for municipality limits considering data fprovided by CIESIN (2021) (c), and distribution of health care centers with antivenom against snakebites in the study area (d).

except the state of Acre. The highest incidence rates were found in the municipalities of Goianorte (Tocantins; 19.55 cases/100,000 inhabitants), Alto Alegre (Roraima; 12.36 cases/100,000 inhabitants), Alto Paraíso (Rondônia; 11.27 cases/100,000 inhabitants) and Presidente Juscelino (Maranhão; 8.41 cases/100,000 inhabitants) (Figure 2b). The highest number of cases were found in Alto Alegre (Roraima), Alto Paraíso (Rondônia), Coari (Amazonas) and Porto Velho (Rondônia), with two cases each. All the other municipalities with cases showed only one case each. We observed no direct relationship between the Elapidae snakebites and human population density ($p > 0.05$). We also did not observe a relationship between Elapidae snakebites with the interaction between human population density and the risk of snakebites ($p > 0.05$). However, we observed a positive and significant correlation with Elapidae snakebites and the risk of snakebites (i.e., suitability value for the presence of Elapidae snakes) ($z = 2.05$, $df = 556$, $p = 0.039$) (Figure 3).

Of the 559 municipalities in the biome, 368 (65.8%) are listed to have health centers with available snake antivenom (Figure 2c). Together, they contain ~18.65 million inhabitants, which represent 83.2% of the population in the area. States with the largest proportional coverage of the population with antivenom were, in decreasing order: Amazonas (98.97%), Pará (96.86%), Roraima (96.8%), Amapá (90.29%), Acre

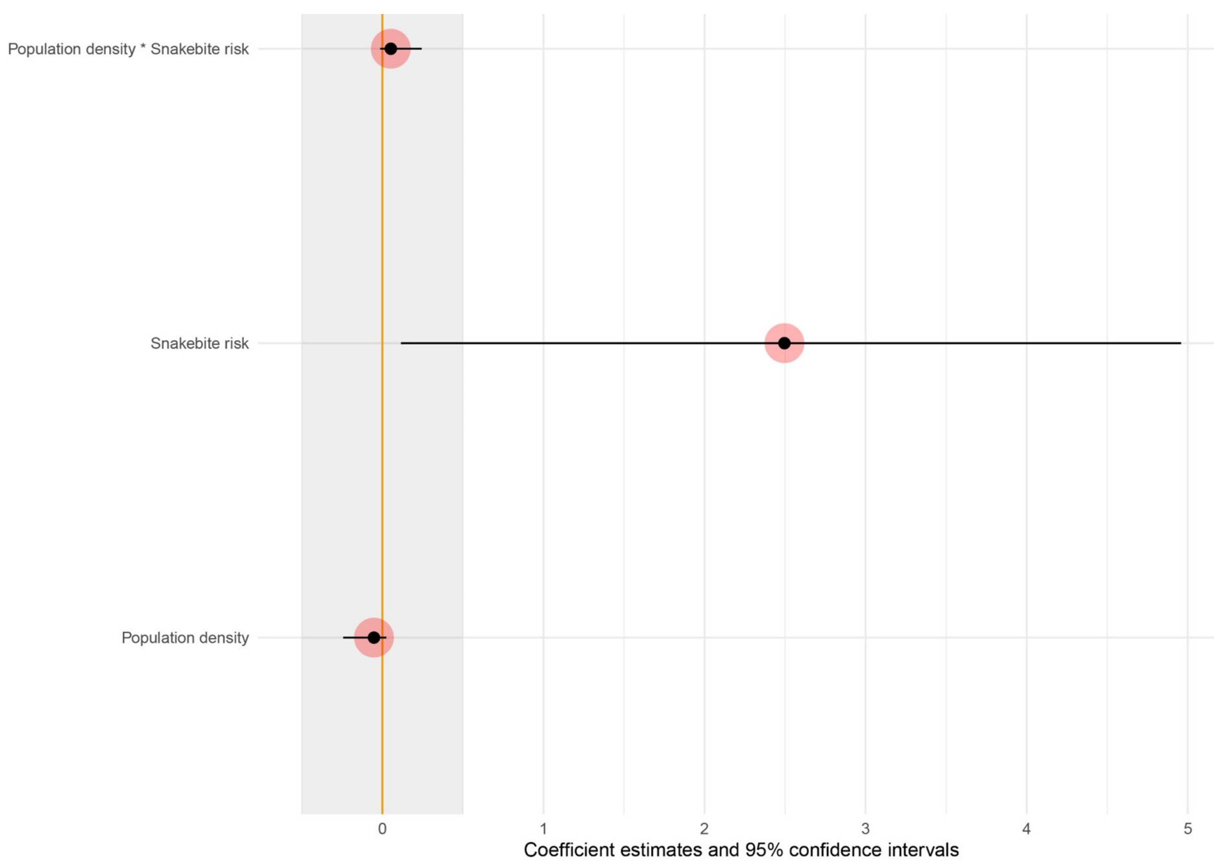

Figure 3. Result of the Generalized Linear Model (GLM): Regression coefficient summary plot for the incidence rate of Elapidae snakebites in Brazilian Amazonia with the interaction between population density and snakebite risk ($p > 0.05$), snakebite risk ($z = 2.05$, $df = 556$, $p = 0.039$) and population density ($p > 0.05$). Points show estimate medians; bars show 95% confidence intervals.

(85.3%), Tocantins (73.18%), Maranhão (68.69%), Rondônia (51.35%) and Mato Grosso (45.82%).

DISCUSSION

Distribution of coral snakes in Amazonia

The main goal of this study was to map the predictive distribution of species of coral snakes in the Brazilian Amazonia. *Micrurus* are mostly small-sized species (snout-vent length ~1000 mm), of secretive/fossorial habits, with few species recorded in urban areas, and the chances of encountering and biting humans, even in densely populated areas, are low (Bisneto et al. 2020a, Marques & Sazima 2021, Risk et al. 2021). Of the 38 species of coral snakes in Brazil, 23 occur in the Amazon region (Nogueira et al. 2019, Costa et al. 2021, Silva Jr. et al. 2021), however, studies on the distribution and/or composition of species in the area tend to be local or regional (e.g. Prudente et al. 2010, Fraga et al. 2013, Bernarde et al. 2017, Silva et al. 2019), which makes it difficult to characterize the real distribution of the coral snakes. We can point out that *Micrurus lemniscatus* is the most recorded coral snake in the area, and despite its widespread distribution, there is a huge gap on its distribution in the southern half of the biome, where it certainly occurs. It is also interesting to note that for most of the suitable areas of *M. annellatus* there is no occurrence record for the species (Figure S1, Supporting information) (Nogueira et al. 2019, Silva Jr. et al. 2021).

Large sampling gaps for *Micrurus* are found in several areas, especially in southern Pará, Amapá, southern Rondônia, Roraima, and southwestern Amazonas (Figure 1a). Many records are close to major cities (e.g., Manaus, Belém) and rivers (e.g. Madeira, Tapajós). In the Amazon, displacement is difficult: frequently there are no roads nearby and many places are days away from the nearest cities, or are in the indigenous territory and/or protected areas, whose biodiversity has been not explored. It is also noteworthy that snakes are inconspicuous animals, difficult to detect and collect (Bernarde et al. 2012, Frazão et al. 2020), especially in densely vegetated tropical forests (Fraga et al. 2014). Small-sized and fossorial/semi-fossorial reptiles, such as *Micrurus* have samples biased (largely toward accessible areas and large population centers) or are under-assessed (Couto et al. 2007, Bland & Böhm 2016, Tingley et al. 2016). Therefore, some studies may simply not have observed the presence of coral snakes, since the low detectability of snakes results in false absences reported by field works (Fraga et al. 2014).

The climatic variables related to the distribution of venomous snake species were mostly associated with temperature and precipitation. Snakes, as ectotherms animals, should be strongly influenced in distribution by the climate, since temperature directly affects their metabolic activity and tend to be more important to reptile species richness (Qian et al. 2007, Kafash et al. 2020). Precipitation can also play an important role in constraining reptiles' activity, distribution, and dispersion (Fraga et al. 2017, Kearney et al. 2018). Climate conditions also seem to modulate the daily activity of at least some species of coral snakes. *Micrurus fulvius* has a peak of activity in the early morning and late afternoon, which indicates that this species avoids the warmer parts of the day (Jackson & Franz 1981), while *Micruroides euryxanthus* is active at night on the surface during or after rains (Vitt & Hulse 1973).

The Brazilian notification system for SBE has a history of underreporting issues (Fiszon & Bochner 2008, Wen et al. 2015) related, for example, to failures during the completion of forms by health professionals (Bernarde 2014). In the case of coral snakes, another problem could be related to confusion with false coral snakes (families Aniliidae, Colubridae, and Dipsadidae; several genera e.g. *Anilius, Apostolepis, Atractus, Erythrolamprus, Oxyrhopus, Phalotris, Phimophis, Pseudoboa*), which in some cases may be responsible for an over-reporting of bites due to both morphological confusion and the fact that they are more common and cause much more bites than coral snakes (Bucaretchi et al. 2021). On the other hand, the need to filter data as we did in this work means that some cases caused by *Micrurus* were left out of the analyses. Another aspect that deserves attention is that of the 14 species analyzed, only half are involved in bites in the region, and only three or four seem to be involved in most of the cases (Bisneto et al. 2020a, b). Many species of *Micrurus* may not influence the risk of bites due to being rarer, having a more restricted geographic range, or being more sensitive to human disturbance — and therefore coming into less contact with humans.

Mapping suitable areas for coral snakes and testing snakebite risk in Amazonia

Our potential distribution models showed high TSS and ROC indices (>0.9), indicating a robustness of the constructed maps (Guisan et al. 2017). Our results indicate that the entire Amazonian biome is suitable for the distribution of coral snakes. Areas with the highest suitability for these venomous snakes are located near major cities like Manaus, Belém, Santarém, and Porto Velho (Figure 2a). As explained above, this may be due to the tendency of rare animals to be found more frequently near large urban centers. However, there are notable exceptions, such as areas in western and northwestern Amazonas, northern Amapá, southern Roraima, and western Marajó island, where urbanization is much more limited. Many species of coral snakes are associated with forests and are hardly found in deforested or urbanized areas (Martins & Oliveira 1998, Santos-Costa et al. 2015, Bisneto et al. 2020a), and those areas may fit in the ecological requirements of the group, even if poorly sampled. In Maranhão state, areas in Amazonia have been associated with higher suitability for coral snakes compared to more open Cerrado areas (Araújo et al. 2022).

Coral snakes is a rich group, able to live in several enviroments, from open to forested areas, in elevation of up to 3,000 m (Marques & Sazima 2021). Most of the species of *Micrurus* are considered either fossorial or subfossorial. A few records of coral snakes climbing vegetation are known, but this behavior is considered rare (Marques & Sazima 2021). In tropical forests in Southeastern Brazil, *Micrurus corallinus* is abundant and seen active on the ground (Marques 1992). In the Amazon some species can coexist, where at least six are recorded for Manaus, Brazil (Dixon & Soini 1986, Martins & Oliveira 1998). Despite the high species richness, the abundance seems to be low in both forested and open areas (Marques et al. 2017, 2019) and aspects of their natural history are not variable among species. *Micrurus* are typically active during the day/night, with few exceptions they feed on similar kind of prey (elongated terrestrial vertebrates) and they are found mainly in areas with forest cover, among leaf litter, in upland or flooded areas (Martins & Oliveira 1998, Duellman 2005, Marques & Sazima 2021). We believe that these aspects support the notion that all the species we considered are biologically similar to consider them together in our results.

Amazonia concentrates about 40% of snakebites in Brazil (SINAN 2022), but it tends to be a wrong number since the lack of detailed data on distribution of snakebites. Most of the data are retrieved for municipalities (Wen et al. 2015, Bisneto et al. 2020b), and not for specific locations (indigenous tribes, riverine communities, smaller towns, etc.). Some of the municipalities show vast territorial limits, and therefore incidence is not always useful in mapping snakebites or risk areas. This issue was already mentioned in studies on snakebites caused by *Bothrops*, the main genus causing snakebites in Brazil (Alcântara et al. 2018). Also, the Amazon shows low populational density along its limits (CIESIN 2021), with sparsely populated settlements surrounded by huge uninhabited areas, and has a huge gap on knowledge of distribution of snakes (Guedes et al. 2018, Nogueira et al. 2019). This makes more refined analyzes of risk areas difficult for this region.

We observed that the potential presence of coral snakes is the only variable that could be associated with risk areas. There was a wide variation in confidence intervals, because in many areas suitable for the occurrence of coral snakes, bites were not recorded, while in others there was a high incidence of SBE. For SBE, assessments of risk areas range from the probability of encounters between humans and venomous snakes (Yañez-Arenas et al. 2018) to analyzes that use ecological data from snakes and socioeconomic data from humans (Martín et al. 2021, 2022). These analyzes have in common the premise that snakebites are dependent on the frequency of contact between humans and snakes (i.e. where there are more humans and snakes, there are more bites) (Bravo-Vega et al. 2019, Martín et al. 2022). In Maranhão, one of the Brazilian states that compose the Amazonian biome, the risk of snakebite had a positive and significant correlation with human population density, but viperids had greater weight in the analyses (Araújo et al. 2022). In Brazil, species of this family, especially from the genus *Bothrops*, are known to be frequently found, in addition to adapting well to altered areas, with some species entering the urban zone (Bernarde 2014). Elapids are difficult to assess by these measures because of their low number of cases (Bisneto et al. 2020a). Another thing that deserves attention is that coral snakes are considered non-aggressive towards people, and have a complex arrange of defensive behaviors that do not include striking and biting (Marques & Sazima 2021), although there are differences between species. In the Amazon, for instance, *M. hemprichii* and *M. lemniscatus* are not considered aggressive, while *M. obscurus* and *M. spixii* show more aggressive behaviours (Buononato et al. 2021). Aggressiveness may be also difficult to analyze because it is a characteristic of individuals, not necesserialy of species. Coral snakes can bite with the slightest provocation (Pardal et al. 2010), while in other cases the snake only bit after being harassed for some time (Bisneto et al. 2023).

In general, states in the area have healthcare centers with antivenom in most (if not all) of their municipalities, and the distribution of healthcare centers tends to follow the distribution of municipalities. Most of the municipalities without antivenom available are small (<20,000 inhabitants). A notable case is Rondônia, whose only half of its population lives in municipalities with health care centers. The population of Mato Grosso inside Amazonia is also poorly covered by healthcare centers. The municipality of Alto Paraíso (Rondônia), had an incidence rate above 11 cases/100,000 inhabitants, however, it does not have a health center with antivenom available (Citeli et al. 2018). It is difficult to access adequate health care in the region: victims of snakebites often seek traditional therapeutic practices or take too long to realize the severity of their cases, which delays or prevent their arrival in health care centers; some of them need to travel for hours/days in various means of transport to reach the health care centers, and not all hospitals officially listed as health centers against snakebites have antivenoms available (Cristino et al. 2021, Salazar et al. 2021). Intensive care units, sometimes needed to assist victims of envenomations by coral snakes, also have low coverage in the area (Bisneto et al. 2020b).

Underreporting of cases or deaths is also a major problem in Amazonia. In some rural areas, most of the victims never reached a health center, so their cases were not reported in the official databases (Salazar et al. 2021). In Brazil, the distribution of antivenoms is based on epidemiological data (Gutiérrez et al. 2009). As a result, decision making regarding the regional distribution of antivenom depends on the number of cases detected by the official surveillance system (Monteiro et al. 2020). However, cases of coral snakes are rare, making it difficult to obtain epidemiological data from them (Bisneto et al. 2020a). Because of that, at least two states (Amapá and Amazonas) have an antivenom distribution policy to provide at least ten vials in each municipality (Deugles Cardoso and Thais Marques, personal communication). Antivenom distribution depends also on the conditions for cold storage and the availability of hospital facilities and proper medical supervision, both unavailable in rural or remote areas of Amazonia. Traditional populations are particularly vulnerable as they are more exposed to bites but have less access to antivenom (Monteiro et al. 2020, Salazar et al. 2021). One option to mitigate these risks is the decentralization of the distribution of antivenom, through production of antivenoms that do not require cold storage (Monteiro et al. 2020).

CONCLUSIONS

The potential distribution maps we provided here should be considered of relevance for public health in Amazonia. They contain geographical information on poorly known venomous snake species in a poorly sampled area. Moreover, they are pioneer in using data of distribution and SBE of a rare group of venomous snakes to assess risk areas for human envenoming involving these species.

All the Amazonian biome is suitable for the occurrence of *Micrurus*, with areas of highest suitability converging to the east. Here, we found that risk areas are those with higher suitability for coral snakes, but this high suitability alone explains very little to the low incidence of cases in the region. States in the area have, in general, good coverage of antivenom, but some states should expand their coverage of healthcare centers to attend to a greater number of inhabitants. Rural and traditional populations are particularly vulnerable due to the unavailability of proper medical care and/or the delay in reaching a health care center. Because of the low incidence of cases and high suitability for coral snakes in the region, antivenom distribution should not be based on epidemiological data, but instead, a minimum supply of antivenom against *Micrurus* should be distributed to all municipalities, including antivenom options that do not require refrigeration for storage.

We recognize the limitations of our study. The low number of snakebites by *Micrurus*, the lack of precise data on where this cases occurred and the known bias on distribution of coral snakes make the mapping of precise risk areas difficult, but we believe that this work can be pioneering because this is the first to point risk areas for coral snakes and raise important issues regarding health care about snakebites in the Amazon region.

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SUPPLEMENTARY MATERIAL

Tables SI-SII

Figures S1-S3

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