Abstract: The coral snake genus *Micrurus* has non-aggressive behavior, being responsible for only 0.4% of the reports of snakebites in Brazil. However, although rare, accidents are potentially serious due to rapidly evolving respiratory paralysis. In the last few years, there was an abrupt reduction in the number of hospitals receiving antivenom support in Rio de Janeiro State, and currently the Health Ministry of Brazil distributes the antivenom only to 25 hospitals in 21 municipalities, even so with no data on specific serum provided by each hospital. This study aimed to determine the potential distribution of *Micrurus* species in Rio de Janeiro State in order
to compare potential areas for risk of elapidic accidents with the localities assisted by hospitals with antivenom distribution. We performed ecological niche models to generate maps of potential distribution for all species through several niche algorithms. Based on these results we analyzed and discussed the consequences of this change in the number of hospitals receiving antivenom. Our results revealed the potential occurrence of the genus throughout the State territory and show a partially homogeneous distribution of health units, although the northern region represents an area with a deficiency in hospital coverage. According to our results and data from the Rio de Janeiro State Secretary of Health, it is highly desirable that at least some antivenom service centers in the regions “Metropolitana” and “Baixadas Litorâneas” receive antielapidic serum and that there be an increase in the number of units in “Norte Fluminense” and “Noroeste Fluminense” regions of Rio de Janeiro State.

Keywords: bioclimatic variables; coral snake; hospitals; niche modeling; snakebite.

INTRODUCTION

Accidents with venomous animals, particularly snakebites, are included by the World Health Organization in the list of neglected tropical diseases affecting, in most cases, poor people living in rural areas with limited and deficient access to health services (Brasil 2015). Estimates point to about 1.8 million people envenomated by snakes in the world, with 94,000 deaths annually (Kasturiratne et al. 2008).

In Brazil, between the years 2001 and 2012, 329,180 cases of snakebites were reported (Bochner et al. 2014). The average number of snakebite incidents during these twelve years were around 27,000, indicating an average increase of 4.1% per year (Bochner et al. 2014). Available data from the years 2009, 2010, and 2011 assert that more than 30,000 cases were registered for treatment during this period (Bochner et al. 2014). During the year of 2016, 26,465 accidents caused by snakes were registered generating 117 deaths in Brazil. Regarding Rio de Janeiro State
510 cases were registered with one confirmed death (these are preliminary data subject to change) (Brasil 2017a).

Popularly known as true coral snakes, *Micrurus* spp. are fossorial or semifossorial, occasionally climbing on vegetation while foraging, and have aposematic color, usually with red, black, and yellow rings organized in different sequences encircling the body (Melgarejo 2003, Campbell & Lamar 2004, Puorto 2012). Most species depend on forest environments and are diurnal, considerably increasing activity after periods of high precipitation during the spring and summer (Campbell & Lamar 2004, Marques *et al.* 2006, Bernarde 2014).


This genus was responsible for 0.6% of snakebite notifications in the country between the years 2001 and 2012 (Bochner *et al.* 2014). According to the most updated and revised data for the year 2013, *Micrurus* caused 240 accidents in Brazil, two of which occurred in Rio de Janeiro State (Brasil 2017a). Due to non-aggressive behavior, small size of their teeth and mouth opening, accidents with *Micrurus* are rare, but potentially serious (Melgarejo 2003, Puorto 2012). Their venom contains neurotoxins and its effects spread rapidly throughout the organism (Silva Jr & Bucaretchi 2003), and the first symptoms may appear in less than one hour after snakebite (Brasil 2001). Lack of adequate treatment may rapidly evolve to respiratory paralysis and even death of the patient (Brasil 2001, Silva Jr & Bucaretchi 2003).

In Brazil, antivenoms are currently produced by Instituto Butantan (São Paulo State), Fundação Ezequiel Dias (Minas Gerais State), Instituto Vital Brazil (Rio de Janeiro State), and
Centro de Produção e Pesquisa em Imunobiológicos (Paraná State). The serum is distributed by the Brazilian Health Ministry, while the Secretaries of Health of each State are responsible for determining the localities that will receive the antivenom (Barbaro 2012). Currently, only Instituto Butantan and Fundação Ezequiel Dias produce specific antivenom for *Micrurus* (antielapidic serum).

According to the Rio de Janeiro State Secretary of Health, in the list available on the Instituto Vital Brazil’s homepage (Rio de Janeiro 2017) one can note that the number of hospitals with antivenom for snakebite has been reduced abruptly in recent years. In 2013, the legally recognized Brazilian antivenom producers simultaneously adjusted and standardized the procedures involved in the manufacture of antivenom in order to comply with a resolution published by the National Health Surveillance Agency (RDC 17/2010) (Brasil 2010). The adequacy process could lead to a shortage of antivenom in Brazil. Therefore, in October 2013 producing institutions proposed to the Ministry of Health the adoption of a shared production program. This request was accepted by the National Health Surveillance Agency in March 2014 and lasted until June 2016 (Brasil 2014). Even with this decision there was a reduction in antivenom production, requiring restructuring of antivenom distribution by the States. As a result, many States, including Rio de Janeiro, reduced the number of antivenom service centers. In 2014, for instance, 61 hospitals in 56 municipalities of Rio de Janeiro State received antivenom for snakebites in general. Currently, only 25 hospitals in 21 municipalities are capable of assistance this type of accident (Brasil 2017b).

The present study aimed to perform ecological niche models to generate maps of potential geographic distribution for four *Micrurus* species occurring in Rio de Janeiro State in order to infer areas with high adequability for this genus and, assuming that all the hospitals listed by the Secretary of Health currently have antielapidic serum, to evaluate the potential effects caused by the reduction of units with snakebite antivenom in the State.
MATERIAL AND METHODS

Antielapidic serum is currently considered to be efficient in the treatment of accidents with any South American species of the genus *Micrurus*. However, recent proteomic studies showed that venom composition of *Micrurus* species is very complex, with even sympatric species showing distinct toxin expression phenotypes (Lomonte *et al.* 2016). Furthermore, the antielapidic serum is not completely effective to neutralize the toxins of the different species of *Micrurus* in Brazil due to variations of venom composition (Tanaka *et al.* 2010). Based on these results we chose to perform ecological niche modeling for each species separately, although our discussion is based on the distribution of the genus in Rio de Janeiro State since the antivenom currently distributed by the Brazilian Health Ministry and Rio de Janeiro State Secretary of Health is the same for all *Micrurus* species.

We searched for target species records (*M. corallinus*, *M. decoratus*, *M. ibiboboca*, and *M. l. carvalhoi*) in the three most important herpetological collections of Rio de Janeiro State: Museu Nacional, Universidade Federal do Rio de Janeiro (MNRJ), Instituto Vital Brazil (IVB), and Instituto de Biologia, Universidade Federal do Rio de Janeiro (ZUFRJ). We also used SpeciesLink (2014) to obtain records from other ten collections (one from Colombia and the others from Brazil): Fundación Puerto Rastrojo (FPR – Colombia), Coleção Científica de Serpentes da Fundação Ezequiel Dias (Funed-Serp – Brazil/MG), Coleção Herpetológica Alphonse Richard Hoge, Instituto Butantan (IBSP-Herpeto – Brazil/SP), Coleção de Répteis do Museu de Biologia Professor Mello Leitão (MBML-Répteis – Brazil/ES), Coleção de Répteis da Pontificia Universidade Católica do Rio Grande do Sul (MCP-Répteis – Brazil/RS), Coleção de Herpetofauna do Museu de Zoologia da Universidade Estadual de Londrina (MZUEL-Herpeto – Brazil/PR), Sistema de Informação do Programa Biota (SinBiota – Brazil/SP), Setor de Herpetologia da Coleção Zoológica da Universidade Federal do Mato Grosso (UFMT-R – Brazil/MT), Zoneamento Ecológico Econômico do Acre (ZEE_Herp – Brazil/AC), and Coleção
de Répteis do Museu de Zoologia da Universidade Estadual de Campinas (ZUEC– REP – Brazil/SP). We chose to include all records in the analysis due to the reduced sample data for some species. The exclusion of this data means to lose important information to build the models. In addition, the number of old records in the database (data from the 1940’s) is extremely low. We obtained the location of occurrence (geographic coordinates) of each specimen directly from collections data. When this information was not available, we obtained the coordinates from digital open-access databases such as Global Gazetteer version 2.2 (Falling Rain Genomics 2010) and Google Earth (Google 2014). All geographic coordinates were converted to the DMS format (decimal degrees) with WGS reference system. For specimens with no exact georeferencing data we considered the central point of the municipality as the valid information. All records were re-examined for possible taxonomic errors and duplicate records were not considered. We calibrated the models using all species distribution area.

Environmental information was obtained from 35 bioclimatic variables available at database WorldClim – 1 to 19 – (Hijmans et al. 2005) and CliMond – 20 to 35 – (Kriticos et al. 2012) plus the altitude variable. We considered environmental layers with spatial resolution of ~1 km since this is the most accurate resolution available and the area considered for analysis is reduced (Rio de Janeiro State). In order to avoid overfitting, Pearson correlation coefficient (r) was calculated between each pair of variables through SPSS software version 17.0 (SPSS Inc 2008), with (r ± 0.7) as cutoff value. Based on these analyses and considering aspects of the biology of the species (Marques et al. 2006), eleven low-correlated variables were selected: altitude, mean annual temperature, temperature seasonality, annual temperature range, driest quarter mean temperature, precipitation seasonality, driest quarter precipitation, the hottest quarter precipitation, radiation seasonality, driest quarter radiation, and mean humidity index of the hottest quarter. These variables combined with specimen coordinates were inserted into five different algorithms for ecological niche modeling. The selected algorithms were Maxent
(Phillips et al. 2006), Bioclim (Busby 1991), BRT (Friedman 2001), RF Random Forests (Breiman 2001) and SVM (Schölkopf et al. 2001, Tax & Duin 2004, Drake et al. 2006), all of them settled to consider 70% of occurrence points as training and 30% as test for model construction. Each model was run 50 times and the model fit was evaluated through the AUC test (Area Under the receiver operating characteristic Curve) for all algorithms and TSS (Total Sum of Squares) for four algorithms except Maxent. The AUC ranges from 0 to 1, where a value of 0.5 denotes a model no better than randomness, while values close to 1 suggest a model capable of perfectly distinguishing between presence and absence records. AUC values ≥ 0.75 point to reliable models (Elith & Burgman 2002). The TSS statistics measures the performance of species distribution models based on presence and absence records independent of prevalence (Allouche et al. 2006). TSS considers both omission and commission errors, and success as a result of random guessing. Values range from −1 to +1, where +1 indicates perfect agreement and values of zero or less indicate a performance no better than random. It is a simple and intuitive measure for the performance of species distribution models when predictions are expressed as presence–absence maps (Allouche et al. 2006). The validation to consider a presence was made by the minimum predicted presence (i.e. the minimal suitability for a real presence record of an individual from our database for each species). The maps generated were inserted into the ArcGIS software version 10.2.2 (ESRI 2014) for image treatment and editing. We considered the presence of a species if its predicted occurrence was corroborated at least by three of the five models generated by different algorithms. The final ensemble showing the sympathy for all analyzed species considered these overlapping presence maps. Hospitals coordinates were determined through Google Earth (Google 2014) and included in the same software for comparisons between the areas of possible occurrence of the genus *Micrurus*.

In 1987 the Government of Rio de Janeiro State approved an Economic and Social Development Plan splitting the territory into eight Government Regions (CEPERJ 2017). Since
then some changes have been made in both the denomination and composition of these Regions, which are currently known as: “Metropolitana”, “Noroeste Fluminense”, “Norte Fluminense”, “Baixadas Litorâneas”, “Serrana”, “Centro-Sul Fluminense”, “Médio Paraíba”, and “Costa Verde” (CEPERJ 2017) (Figure 1A). We adopted this nomenclature to easily refer to the distribution of hospitals throughout Rio de Janeiro State.

RESULTS

We obtained records of 753 specimens (476 *M. corallinus*, 57 *M. decoratus*, 37 *M. ibiboboca*, and 183 *M. l. carvalhoi*). The mean AUC value for the four species were higher than 0.75 in all models: *Micrurus corallinus* (Maxent 0.992, Bioclim0.770, BRT 0.999, RF 0.998, and SVM 0.998); *M. decoratus* (Maxent 0.998, Bioclim 0.800, BRT 0.999, RF 0.999, and SVM 0.997); *M. ibiboboca* (Maxent 0.996, Bioclim 0.890, BRT 0.957, RF 0.969, and SVM 0.918); and *M. lemniscatus carvalhoi* (Maxent 0.985, Bioclim 0.809, BRT 0.850, RF 0.889, and SVM 0.862), indicating a high predictive power of the different models. Additionally, mean TSS values also indicated performances better than random: *Micrurus corallinus* (Maxent NA (not applicable), Bioclim -0.23, BRT 0.84, RF 0.92, and SVM 0.92); *M. decoratus* (Maxent NA, Bioclim -0.65, BRT 0.96, RF 0.96, and SVM 0.96); *M. ibiboboca* (Maxent NA, Bioclim -0.75, BRT 0.55, RF 0.73, and SVM 0.52); and *M. lemniscatus carvalhoi* (Maxent NA, Bioclim-0.35, BRT 0.71, RF 0.58, and SVM 0.67). The distribution models of *M. corallinus*, *M. decoratus*, and *M. l. carvalhoi* showed the potential occurrence of these taxa throughout Rio de Janeiro State. Regarding *M. ibiboboca* there is high suitability of occurrence only in the coastal zone of the State (Figure 2). With the aid of the Maxent algorithm it is also possible to know which bioclimatic variables contributed the most to each distribution model generated (Table 1).

The “Norte Fluminense” region was deficient in relation to hospital coverage even before the reduction of the units with snake antivenom. However, after the extinction of 36 health units,
the regions known as “Noroeste Fluminense”, “Serrana”, “Centro-Sul Fluminense”, and “Médio Paraiba” were also affected (Figure 1B).

Table 1. Relative importance of bioclimatic variables in the distribution models generated for each species of Micrurus with the software Maxent.

<table>
<thead>
<tr>
<th>Bioclimatic Variables</th>
<th>Micrurus corallinus</th>
<th>Micrurus decoratus</th>
<th>Micrurus ibiboboca</th>
<th>Micrurus l. carvalhoi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altitude</td>
<td>0.5</td>
<td>7.5</td>
<td>7.9</td>
<td>3.4</td>
</tr>
<tr>
<td>Mean annual temperature</td>
<td>3.2</td>
<td>1.4</td>
<td>7.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Temperature seasonality</td>
<td>16.6</td>
<td>16.5</td>
<td>51.3</td>
<td>17.1</td>
</tr>
<tr>
<td>Annual temperature range</td>
<td>18.2</td>
<td>0.2</td>
<td>6.4</td>
<td><strong>29.5</strong></td>
</tr>
<tr>
<td>Driest quarter mean temperature</td>
<td>4.4</td>
<td>0.4</td>
<td>0.1</td>
<td>5.0</td>
</tr>
<tr>
<td>Precipitation seasonality</td>
<td>0.6</td>
<td>4.6</td>
<td>0.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Driest quarter precipitation</td>
<td>12.1</td>
<td>7.1</td>
<td>1.8</td>
<td>2.2</td>
</tr>
<tr>
<td>The hottest quarter precipitation</td>
<td>6.4</td>
<td>22.1</td>
<td>9.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Radiation seasonality</td>
<td>7.2</td>
<td>1.0</td>
<td>5.1</td>
<td>10.7</td>
</tr>
<tr>
<td>Driest quarter radiation</td>
<td>6.9</td>
<td>0.1</td>
<td>0.1</td>
<td>6.2</td>
</tr>
<tr>
<td>Mean humidity index of the hottest quarter</td>
<td><strong>23.7</strong></td>
<td><strong>39.1</strong></td>
<td>10.6</td>
<td>19.9</td>
</tr>
</tbody>
</table>

Variables with the highest relative contributions are in bold.
Figure 1. (A) Government Regions of Rio de Janeiro State. (B) Potential distribution and sympatry of the four species predicted by at least three different models pooled together with the distribution of health units in Rio de Janeiro State. All hospitals plotted on the map had antivenoms in 2014. In green are the hospitals that no longer receive antivenom and in blue are those that continue to receive antivenom.
The only government official data available on hospitals receiving snake antivenom is the list of Instituto Vital Brazil’s homepage which contains only the addresses and telephones of these hospitals, with no information on the specificity of the antivenoms. We insistently looked for this information through literature data and contacts with the Rio de Janeiro State and Municipal Secretaries of Health, but we were not successful.

Even if all hospitals have antielapidic serum, the distribution of health units would still be only partially homogeneous when compared to the potential distribution of *Micrurus* spp. in Rio de Janeiro State. As we can see in Figure 1B, there is a deficiency of hospitals in the “Noroeste Fluminense” and “Norte Fluminense” regions of the State. The only data we are aware of regarding the distribution of antielapid serum is a presentation on surveillance of accidents caused by venomous animals attended by one of us (C. Machado) and organized by the Ministry of Health in August 2017, in the municipality of Niterói. In this event, data from the Rio de Janeiro State Secretary of Health indicated that the only service centers currently receiving antielapidic serum are located in the municipalities of Angra dos Reis, Paraty, Vassouras, and Volta Redonda, and even then, with an amount only sufficient for a single treatment. These municipalities comprise only the following government regions: “Costa Verde”, Médio Paraiba”, “Centro-Sul Fluminense”, and “Serrana”.
DISCUSSION

Distribution models

The high AUC and TSS indexes indicate that the actual distribution areas of this species were estimated with more than 75% of accuracy (Elith et al. 2006). Although the variable ‘altitude’ presented less contribution in the distribution of *M. decoratus* as pointed in Table 1, a review of the geographic distribution of the species reinforces the hypothesis that this taxon inhabits areas of plateaus and mountains (Gonzalez et al. 2014). The high suitability potential in altitude areas pointed out by the model, as one can notice in Figure 2, cannot be explained by the
direct influence of the altitude variable but by the influence of altitude in other correlated variables.

**Antivenom availability**

Snakebites are medical emergencies that require prompt medical attention. Thus, the most important issue for reducing their biosocial impact is a rapid access to effective healthcare (Gutiérrez et al. 2015). Considering that species of *Micrurus* depend on forested environments (Campbell & Lamar 2004) and that the generated models indicate the potential occurrence of the genus throughout Rio de Janeiro State, casual encounters of these snakes with humans, although rare, may occur and result in accidents (Brasil 2001). These results coupled with the severity of the intoxication and also rapid worsening of the clinical picture of an elapidic accident (Melgarejo 2003), demand a homogeneous and efficient distribution of antielapidic antivenom throughout Rio de Janeiro State.

The time between the accident and the antivenom administration is the main factor contributing to high rates of lethality (Mota-da-Silva et al. 2015). Studies before 2012 indicate that the average time between accident and first aid for the victim in Rio de Janeiro State was better than that recommended by the Ministry of Health (less than six hours), with only 4.8% of the cases being treated after this time interval and almost all cured (Machado et al. 2012). However, the current framework can be drastically changed since the number of hospitals able to assist accidents with snakes has been reduced to less than half compared to 2014. Despite being a very small sample, the preliminary Sinan data (Brazil 2017a) already shows a disturbing alteration between the time of the accidents with *Micrurus* and the medical attention in Rio de Janeiro State. In 2014 there were three accidents: one attended in less than one hour and two others whose timeframe was not disclosed. In 2016 there were four accidents: two between one
and three hours, one between three and six hours and one without available information (Brazil 2017a).

Supposing the ideal scenario in which all the hospitals have antielapidic serum, one can notice that an increase in the number of units in “Norte Fluminense” and, in particular, “Noroeste Fluminense” regions of Rio de Janeiro State is still imperative. These two regions together have 22 municipalities and four hospitals (“Norte Fluminense” – eight municipalities and three hospitals, “Noroeste Fluminense” – 14 municipalities and one hospital). In these regions the distance between the nearest hospitals (both in the same region – “Norte Fluminense”) is 38.5 km while between the more distant hospitals is 209 km. The only hospital in “Noroeste Fluminense” is, at least, 104 km from any other hospital of Rio de Janeiro State. Therefore, accidents occurring in these places cause the victim to be transported by many kilometers until arriving at a primary health post. Thus, as mentioned above, an increase in the time to start treatment also leads to an increase in the risks of sequelae or death (D’Agostini et al. 2011). Considering that accidents with *Micrurus* represent only 0.4% of total accidents currently in the country (Brasil 2001), the distribution of antielapidic antivenom to all hospitals is not necessary. However, the responsible authorities should undertake deeper studies, considering the maximum time of patient displacement between health units, in order to develop an efficient distribution of antielapidic antivenom. In particular, according to our results and data from the Secretary of Health of Rio de Janeiro State, it is highly desirable that at least some antivenom service centers in the regions “Metropolitana” and “Baixadas Litorâneas” also receive antielapidic serum. Besides, health units also require appropriate storage infrastructure, access to complementary medications, equipment needed to administer the antivenom, and knowledge of the medical team in identifying the type of envenomated to administer the appropriate antivenom (Gutiérrez et al. 2015).

Despite the high numbers of reported snake accidents, the real magnitude of epidemiological data is still inconsistent throughout Brazil due to the large number of
underreporting and omissions of data in the completion of many fields of the investigation form (Machado 2016). The Ministry of Health (Brasil 2001) has statistical data showing that this underreporting may indicate failures in the health system. As most of the population affected by this affliction corresponds to a low socioeconomic status and, consequently, has little political influence, Neglected Tropical Diseases have low impact on the public health policies priorities (Machado 2016). This implies low investments in research, fragility and inefficiency of epidemiological information, reinforcing the perpetuation of poverty conditions and precarious health conditions (Machado 2016).

Studies using niche modeling to estimate snakebite risks in South America are still scarce. Yañez-Arenas et al. (2018) identified vulnerable human communities to snakebites in Ecuador and commented on the success of ecological niche modeling to infer geographic patterns of ophidism at continental, national and regional scales. The authors also discuss the importance of this kind of studies when hospital data are scarce or biased, highlighting the importance of conducting studies to evaluate which factors contribute the most to snakebite risk and suggesting that anthropogenic climate change should be considered to anticipate strategies for antivenom distribution. The conclusions of Yañez-Arenas et al. (2018) are very similar to data presented herein and reinforces that epidemiology of venomous snakes is an urgent matter that should be widely discussed in the scientific community, regardless of the geographic scale in question. It is also fundamental that researchers, health professionals and public health education institutions have government support and information, so that snake accidents cease to be a neglected disease and reduce impacts on the population.

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