ORIGINAL ARTICLE / ARTIGO ORIGINAL

Epidemiology of envenomation by Africanized honeybees in the state of Rio Grande do Norte, Northeastern Brazil

Epidemiologia dos envenenamentos por abelhas africanizadas no Estado do Rio Grande do Norte, Nordeste do Brasil

Michael Radan de Vascon	icelos Marques ⁱ 🗓, Kaliany <i>i</i>	Adja Medeiros de Araújo [,] 📵,
Aluska Vieira Tavares ⁱ 🕒	, Alecxandro Alves Vieira ^ı 🝺	, Renner de Souza Leite ⁱ 🗓

ABSTRACT: *Introduction:* In the American continent, accidents caused by honeybees are a public health problem due to the high incidence and severity of the cases. Despite its medical importance, there are few epidemiological studies on this topic in Brazil, especially referring to the Northeastern states. The present study aims to describe the epidemiological features of honeybee envenomation cases in the state of the Rio Grande do Norte, Northeastern Brazil, from 2007 to 2014. *Methods:* Data were collected from the Notifiable Diseases Information System database of the Health Department of Rio Grande do Norte. *Results:* We analyzed a total of 2,168 cases. Cases occurred in all months of the years studied, reaching higher frequencies from June to October. Most incidents happened in urban areas and involved men, with victims aged between 20 and 39 years. Victims were mainly stung on the head and hand, and they received medical care predominantly within 3 hours after the injury. Local manifestations were more frequent than systemic ones. Clinically, most cases were mild and progressed to cure. *Conclusion:* The high number of honeybee sting cases shows that Rio Grande do Norte may be an important risk area for such injury.

Keywords: Bees. Poisoning. Poisonous animals.

'Centro de Educação e Saúde, Unidade Acadêmica de Saúde, Graduate Program in Natural Sciences and Biotechnology, Universidade Federal de Campina Grande — Cuité (PB), Brazil.

Corresponding author: Michael Radan de Vasconcelos Marques. Unidade Acadêmica de Saúde, Centro de Educação e Saúde, Universidade Federal de Campina Grande, Olho D'água da Bica, s/n., CEP 58175-000, Cuité, PB, Brasil. E-mail: michael.radan@bol.com.br Conflict of interests: nothing to declare – Financial support: none.

RESUMO: *Introdução:* No continente americano, os acidentes causados por abelhas são um problema de saúde pública devido à alta incidência e severidade dos casos. Apesar de sua importância médica, há poucos estudos epidemiológicos sobre esse tema no Brasil, especialmente referentes aos estados do Nordeste. O presente estudo tem como objetivo descrever as características epidemiológicas dos casos de envenenamento por abelhas no estado do Rio Grande do Norte, no Nordeste do Brasil, de 2007 a 2014. *Metodologia:* Os dados foram coletados da base de dados do Sistema de Informação de Agravos de Notificação da Secretaria Estadual de Saúde do Rio Grande do Norte. *Resultados:* Um total de 2.168 casos foram analisados. Os casos mostraram distribuição em todos os meses dos anos estudados, com maior frequência de junho a outubro. A maioria dos casos ocorreu em áreas urbanas e envolveu homens, com vítimas entre 20 e 39 anos de idade. As vítimas foram principalmente picadas na cabeça e na mão, e receberam assistência médica predominantemente dentro de 3 horas após serem picadas. As manifestações locais eram mais frequentes do que as sistêmicas. Clinicamente, a maioria dos casos foi leve e progrediu para cura. *Conclusão:* O alto número casos de picadas de abelhas mostra que o Rio Grande do Norte pode ser uma importante área de risco para tal incidente.

Palavras-chave: Abelhas. Envenenamento. Animais peçonhentos.

INTRODUCTION

From 1840, bees of European — German (*Apis mellifera mellifera*) and Italian (*Apis mellifera ligustica*) — origin were brought to Brazil for apiculture. These honeybees do not exhibit defensive behavior, produce little honey, and have difficulty adapting to the Brazilian environmental conditions. In 1956, honeybees from Africa (*Apis mellifera scutellata*)¹ were introduced in Brazil to improve honey production. This species is characterized by a great capacity to produce honey, a highly defensive behavior, and its easy adaptation to the climatic conditions of the American continent¹²². In 1957, some African queen bees accidentally escaped into the environment, leading to the crossing in nature between African and European bees, which created the Africanized bees². Africanized bees rapidly migrated to other regions of the American continent, reaching the USA in 1990³.

Africanized bees are excellent producers of honey, but they exhibit intense defensive responses. In addition, they present swarming behavior, are persistent when attacking the invader, and reproduce quickly². Because of these characteristics, Africanized bees have frequently been involved in cases of human accidents. These cases can often be severe and lead to death, especially among children and older adults⁴. Thus, such accidents have been considered a public health problem in several American countries, particularly in Brazil²-⁴. Clinically, honeybee stings manifest themselves depending on the individual's sensitivity to venom and number of stings⁴-⁵. Reactions may be local, allergic, and/or toxic. The local reaction is limited to the injury site and has no systemic repercussions. In this case, hospital admission is not necessary to monitor the victim⁴. The allergic reaction, also known as type I hypersensitivity reaction, occurs when the individual presents an allergic response with IgE

antibody production against venom fractions. In this case, a single sting can cause a severe clinical condition, with the onset of glottic edema or anaphylactic shock⁴. Envenoming results from the massive attack of bees, in which the individual gets multiple stings. Systemic injury occurs due to the high amount of venom inoculated into the blood of the victim^{4,5,12,25}.

Accidents with honeybees increased in all regions of Brazil, from 1,440 cases in 2000 to 12,072 in 2016. Mortality also increased from 3 deaths in 2000 to 31 in 2016. The Southeast region recorded the highest number of cases (n = 5,304), followed by the Northeast (n = 3,309), South (n = 2,387), North (n = 557), and Midwest (n = 528). Despite its medical importance, epidemiological studies on honeybee accidents in Northeastern Brazil are still scarce, cases are often underreported, and data collection is poor. In addition, social and environmental changes that have taken place in this region during the last decades indicate that further research is essential to improve knowledge of this topic. In this regard, the present study aims to determine the epidemiological characteristics of cases of honeybee envenomation in the state of Rio Grande do Norte, Northeastern Brazil, from 2007 to 2014.

METHODS

STUDY AREA

The state of Rio Grande do Norte is located in the Northeast of Brazil and has an area of $52,811,126 \text{ km}^2$, distributed in 167 cities. Natal is the capital of the state and has the highest number of inhabitants of the state. The cities were grouped into four regions: *Oeste Potiguar, Central Potiguar, Agreste Potiguar,* and *Leste Potiguar*^{7,8}. Estimates indicate that Rio Grande do Norte has 3,168,027 inhabitants, with about 77.8% of the population living in urban areas and 22.2% in rural areas. Regarding gender, the number of women is slightly higher (n = 1,619,140) than that of men (n = 1,548,887). Most of Rio Grande do Norte has semi-arid climate, with low and irregular precipitation during the year. The state also displays tropical climate, predominantly on the East coast, where rainfall is more frequent. Due to the prevalence of the semi-arid climate and the low rainfall indices, the vegetation that best adapted to the climatic conditions was the *caatinga*. The average annual temperature is around 26° C, with a maximum of 31° C and a minimum of 21° C¹⁰. The rainy season begins in April and ends in July¹¹.

DATA COLLECTION

Honeybee sting cases are required to be notified to the National Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação* — SINAN). SINAN is a software that integrates a database with records of various diseases and health problems that require more detailed monitoring. These injuries cover accidents with venomous animals.

The present study included all cases of injury involving bees treated in the public health system of Rio Grande do Norte and recorded in SINAN from January 2007 to December 2014. We analyzed the epidemiological data according to the month, year, and city of occurrence, gender and age of the victim, area of occurrence (urban or rural) of the case, anatomical sting site, interval between the sting and medical care, case severity and progression, and presence of local and systemic manifestations.

SPATIAL DISTRIBUTION

The map was developed using the QGIS 2.8 software. We calculated the incidence based on the number of bee accidents by the population of each city, with an estimated population of 100,000. The spatial interpolation of the incidence of cases was mapped using data from the 167 cities, using the inverse distance weighting method⁷.

STATISTICAL ANALYSIS

We performed the statistical analyses using the SPSS software, version 22.0 (Statistical Package for the Social Sciences), for Windows. The chi-square test tested the association among variables. Odds ratio was used to measure the effect. We conducted the ANOVA test to analyze the variation of the mean of accidents between the months of the year. The significance level adopted was p < 0.05.

ETHICAL CLEARANCE

Even though we only analyzed the secondary data provided by SINAN, with no identification of the victims, the present study was submitted to and approved by the Research Ethics Committee of the Universidade Federal de Campina Grande, under no. 1,707,234/2016, and followed the guidelines established by the Declaration of Helsinki.

RESULTS

SPATIAL DISTRIBUTION

Incidence rates were unevenly distributed across Rio Grande do Norte, although honeybee sting cases were reported in the 47 cities. The mapping showed a large area with high incidence rates in the central and west regions of the state. The cities with the highest incidence of cases were: Pau dos Ferros, Guamaré, Patu, Riacho de Santana, Acari, Mossoró, Parelhas, Cerro Corá, Ceará Mirim, and Caraúbas (Figure 1).

EPIDEMIOLOGICAL CHARACTERISTICS

A total of 2,168 cases were recorded by the Health Department of Rio Grande do Norte from January/2007 to December/2014, representing an average of 271 cases per year. The mean incidence rates per 100,000 inhabitants were 0.5, 2.3, 4.2, 5.2, 13.8, 8.9, 10.3, and 20.8 cases from 2007 to 2014, respectively. The number of cases gradually increased

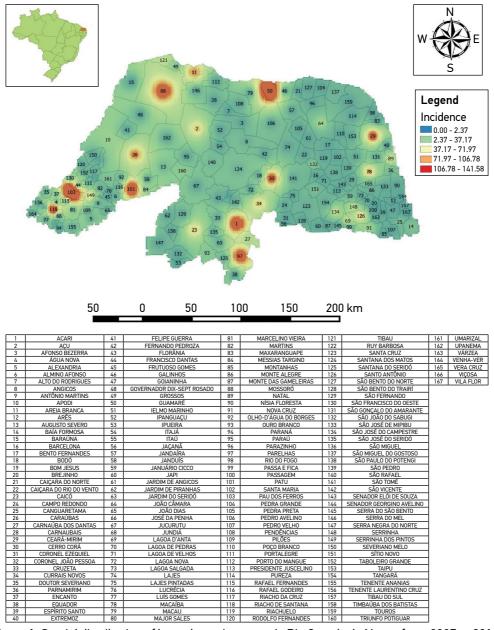
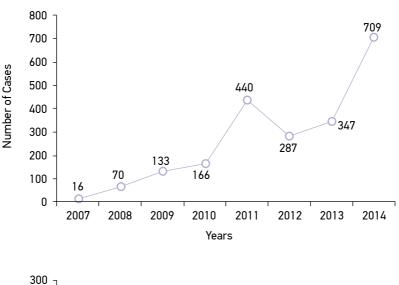


Figure 1. Spatial distribution of honeybee sting cases in Rio Grande do Norte, from 2007 to 2014.

during the investigated period: from 16 cases in 2007 to 709 cases in 2014 (Figure 2A). Figure 2B shows that cases were reported in all months of the years studied, with a small increase between June and October (n = 1,071; 49.4%), followed by a gradual decrease from December to May (n = 590; 27.2%). October (n = 239; 11.7%) and March (n = 144; 6.6%) were the months with the higher and lower number of cases, respectively. Despite the slight increase in cases between June and October, the ANOVA test showed no significant variation between the months of each year (p = 0.975). Table 1 shows that the frequency of cases was higher among men (n = 1,389; 64.1%) than women (n = 779; 35.9%). The highest frequency of stings involved individuals aged between 20 and 29 years (n = 600; 27.6%), followed by the age group 30 to 39 years (n = 422; 19.46%). Age groups 40 to 49 years and



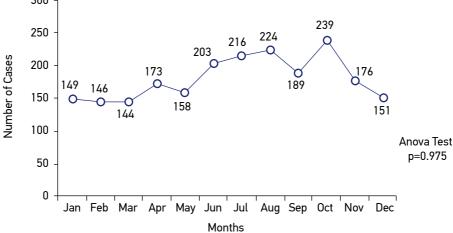


Figure 2. (A and B) Temporal distribution of honeybee sting cases in Rio Grande do Norte, from 2007 to 2014.

Table 1. Distribution of honeybee sting cases in Rio Grande do Norte, from 2007 to 2014, according to gender, age, area of occurrence, anatomical sting site, and interval between the sting and medical care.

Variables	Gen	Gender	
	Male 1,389 (64.1%)	Female 779 (35.9%)	Total 2,168 (100%)
Age group			
1–9 years	193 (8.9)	119 (5.5)	312 (14.4)
10–19 years	175 (8.1)	111 (5.1)	286 (13.2)
20–29 years	380 (17.5)	220 (10.1)	600 (27.6)
30–39 years	284 (13.1)	138 (6.4)	422 (19.5)
40–49 years	168 (7.7)	96 (4.4)	264 (12.1)
50–59 years	67 (3.1)	45 (2.1)	112 (5.2)
≥ 60 years	122 (5.7)	50 (2.3)	172 (8.0)
Area of occurrence			
Urban	909 (41.9)	517 (23.8)	1,426 (65.7)
Rural	300 (13.8)	174 (8.0)	474 (21.8)
Peri-urban	16 (0.7)	16 (0.7)	32 (1.4)
Unknown	164 (7.7)	72 (3.4)	236 (11.1)
Anatomical sting site			
Head	517 (23.8)	187 (8.7)	704 (32.5)
Arm	169 (7.8)	119 (5.5)	288 (13.3)
Hand	159 (7.3)	136 (6.2)	295 (13.5)
Trunk	114 (5.3)	50 (2.3)	164 (7.6)
Leg	47 (2.2)	54 (2.5)	101 (4.7)
Foot	58 (2.7)	64 (2.9)	122 (5.6)
Unknown	325 (15.0)	169 (7.8)	494 (22.8)
Interval between the sti	ng and medical care		'
0–1 h	404 (18.6)	188 (8.7)	592 (27.3)
1–3 h	277 (12.8)	152 (7.0)	429 (19.8)
3–6 h	73 (3.4)	58 (2.7)	131 (6.1)
6–12 h	38 (1.7)	29 (1.3)	67 (3.0)
12–24 h	86 (4.0)	59 (2.7)	145 (6.7)
> 24 h	93 (4.3)	86 (4.0)	179 (8.3)
Unknown	418 (19.3)	207 (9.5)	625 (28.8)

over 60 years were more associated with moderate/severe cases (χ^2 test between severity and age: p = 0.000). The frequency of cases was higher in urban (n = 1,694; 78.1%) than rural areas (n = 422; 19.46%). Accidents in rural areas were more severe (χ^2 test between severity and area of occurrence: p = 0.000; OR = 0.371; 95%CI 0.245 – 0.561). The most common anatomical sting site was the head (n = 704; 32.4%), followed by hand (n = 226; 10.4%), and arm (n = 204; 9.41%), but the body regions affected that resulted in severe cases were the head and trunk (χ^2 test between severity and anatomical sting site: p = 0.026; 95%CI 0.023 - 0.029). The most frequent interval between the sting and medical care was up to 1 hour after the incident (n = 592; 27.3%). Table 2 shows that most cases were classified as mild (n = 1,887; 87.0%), while some were moderate (n = 104; 4.8%), and a few were severe (n = 8; 0.4%). Most cases progressed to cure (n = 1,914; 88.3%), and three individuals died, resulting in the lethality rate of 0.14%. Table 3 shows that the most frequent local manifestations were pain (n = 1,640; 86.6%), edema (n = 1,557; 82.2%), itching (n = 112; 5.9%), and ecchymosis (n = 63; 3.3%), whereas the most frequent systemic manifestations were headache (n = 34; 18.0%), vagal (n = 30; 15.8%), dyspnea (n = 28; 14.8%), fever (n = 27; 14.3%), and neuroparalytic manifestations (n = 13; 6.8%).

DISCUSSION

In Brazil, 74,352 honeybee sting cases were reported from 2007 to 2014^6 . The Southeastern region has the highest number of cases, followed by the Northeastern region. Rio Grande do Norte is the Northeastern state with the highest incidence and the third Brazilian state most

Table 2. Distribution of honeybee sting cases in the state of Rio Grande do Norte, from 2007 to 2014, according to case severity and progression.

Variables	Gender		Takal	
	Male 1,389 (64.1%)	Female 779 (35.9%)	Total 2,168 (100%)	
Severity				
Mild	1,197 (55.1)	690 (31.8)	1,887 (87.0)	
Moderate	75 (3.5)	29 (1.3)	104 (4.8)	
Severe	08 (0.4)	00 (0.0)	08 (0.4)	
Unknown	109 (5.1)	60 (2.8)	169 (7.8)	
Progression				
Death	03 (0.1)	00 (0.0)	03 (0.1)	
Cure	1,211 (55.9)	703 (32.4)	1,914 (88.3)	
Unknown	175 (8.1)	76 (3.5)	251 (11.6)	

affected by this type of injury, after Roraima (first) and Tocantins (second), both from the Northern region⁶. The present study shows that the cases of accidents with bees increased in Rio Grande do Norte: from 16 cases in 2007 to 709 in 2014, with a total of 2,168 incidents. These data are in agreement with those provided by the Brazilian Ministry of Health (n = 2,191). This small difference in the number of cases has been reported in epidemiological studies with venomous animals^{7,8,12}. This finding may be due to possible failures in filling the record forms and data processing between the health departments of the cities, the state, and, finally, the Ministry of Health.

The cases of honeybee accidents occurred in all months of the years analyzed. Although the interval between June and October shows more cases, the results indicate that the accidents were not seasonal. However, there is evidence of seasonality in accidents with other venomous animals (snakes and scorpions)¹³. The increase in

Table 3. Distribution of honeybee sting cases in the state of Rio Grande do Norte, from 2007 to 2014, according to local and systemic manifestations.

Variables	Gender		
	Male	Female	Total
Local manifestations	1,203 (63.5%)	690 (36.5%)	1,893 (100%)
Necrosis	03 (0.2)	01 (0.1)	04 (0.3)
Paresthesia	13 (0.7)	09 (0.5)	22 (1.2)
Ecchymosis	42 (2.2)	21 (1.1)	63 (3.3)
Itching	66 (3.5)	46 (2.4)	112 (5.9)
Edema	1,006 (53.1)	551 (29.1)	1,557 (82.2)
Pain	1,042 (55.0)	598 (31.6)	1,640 (86.6)
Systemic manifestations	112 (59.3%)	77 (40.7%)	189 (100%)
Hemorrhagic	00 (0.0)	00 (0.0)	00 (0.0)
Renal	04 (2.1)	00 (0.0)	04 (2.1)
Dizziness	06 (3.2)	00 (0.0)	06 (3.2)
Myolytic/hemolytic	08 (4.2)	02 (1.1)	10 (5.3)
Nausea	05 (2.6)	08 (4.2)	13 (6.8)
Neuroparalytic	08 (4.2)	05 (2.6)	13 (6.8)
Fever	16 (8.5)	11 (5.8)	27 (14.3)
Dyspnea	17 (9.0)	11 (5.8)	28 (14.8)
Vagal	15 (7.9)	15 (7.9)	30 (15.8)
Headache	21 (11.1)	13 (6.9)	34 (18.0)

the incidence of these injuries often coincides with the rainy season in the Northeast, which corresponds to April to July¹⁴. However, this fact does not apply to honeybees as they tend not to leave their hives during the rainy season¹⁵. The analysis of the spatial distribution of bee stings showed that the cities with the highest incidence are located in the central and western regions of the state. These regions are in semi-arid areas where the dry climate prevails for about 7 to 8 months, with high temperatures and low precipitation¹⁶. Bees may come out of their hives when the weather is very dry and hot, looking for shading from the trees and installing their hives in other locations. In this scenario, they seek better survival conditions, where the availability of water and food is greater. The higher movement of bees may contribute to increasing the incidence of accidents. In addition, the central and western regions have many apiaries, bearing in mind that Rio Grande do Norte is one of the largest honey producers in the country¹⁷. These results suggest that the central and western regions of the state may be a risk area for honeybee accidents. The present study showed that the incidence was low in coastal areas, ranging from 0 to 2.4 cases per 100,000 inhabitants per year. In these areas, the number of accidents may be lower due to the high precipitation and relative humidity of the air¹⁸. A study has reported a positive relationship between average temperature and the migratory process of bees and that rainfall and relative humidity are negatively related to this process¹⁵. The greater number of inhabitants in these areas and the high capacity of bees to adapt to anthropogenic environmental changes¹⁹ may explain the predominance of accidents in urban areas (65.7%). Social and environmental changes, as well as the behavior of humans, imposing their changes in rural areas, reduce the quality and availability of habitats for bees, promoting more frequent contact between honeybees and humans²⁰. Consequently, urban areas often become a refuge and shelter in situations of threat to bees, besides being a place with a high source of food in times of scarcity²¹. Although apiculture is practiced in rural areas, these locations did not have a high number of cases. Only 4% of the cases were work-related, indicating that the accidents may be associated with the dispersal behavior of the bees to urban areas. The area of occurrence of the accident showed a strong association with the presence of systemic manifestations (χ^2 test between systemic manifestations and area of occurrence p = 0.000; OR = 0.450; 95%CI 0.319 – 0.634) and severity (χ^2 test between severity and area of occurrence: p = 0.000; OR = 0.371; 95%CI 0.245 – 0.561). Moderate and severe cases were more associated with accidents occurring in rural than urban areas. This increase in severity may be due to the greater difficulty of the population in accessing health care services. On the other hand, cases in the urban area have a lower risk of systemic manifestations and progression to greater severity.

Most cases affected the male gender (64.1%). These results are in agreement with other studies carried out in the Northeast in which the percentage of men stung by bees ranged from 63 to $68.2\%^{12,19,24,26}$. The gender of the victim is associated with the severity of the case (p = 0.022; OR = 1.65; 95%CI 1.070 – 2.544). In this analysis, men are about twice as likely to exhibit moderate or severe clinical conditions than women. The literature has

reported that the male-female ratio in Hymenoptera accidents is 2:1. Men are more susceptible to severe conditions due to allergic reactions²². The age group most affected was 20 to 39 years, that is, the economically active population. The analysis of epidemiological data on accidents with venomous animals carried out by the Brazilian Ministry of Health in 2014⁶ corroborates this result. Individuals aged 40 to 49 years and older than 60 years are more associated with moderate or severe cases (χ^2 test between severity and age: p = 0.000; 95%CI 0.000 - 0.000). In addition, in individuals older than 60 years, the percentage of moderate or severe cases is about three times greater than mild cases. This situation may occur because individuals over 60 years are in the process of metabolic decline, decreased physiological functions, loss of muscle mass, and reduced resistance to physical and chemical injuries²³.

Regarding the anatomical sting site, the most affected body part was the head (32.4%). This result is in agreement with epidemiological studies on bees carried out in the Northeast region, where the percentage of victims stung in the head is high, varying between 30 and 40%^{12,24}. Bees, being winged insects, preferentially attack the upper regions of the body, such as head and trunk. We found a strong association of the anatomic sting site with the presence of systemic manifestations (χ^2 test between systemic manifestations and anatomical sting site: p = 0.015; 95%CI 0.013 - 0.017). The head and trunk are the sites most associated with such manifestations. In addition, we identified a significant relationship between the anatomical sting site and severity (χ^2 test between severity and anatomical sting site: p = 0.026; 95%CI 0.023 – 0.029). In this analysis, cases in which the individuals were stung in the head and trunk showed greater severity. Santana and Suchara reported that the proximity of the sting site to vital organs determines a greater severity of the clinical condition. When the sting occurs in the head, the symptoms are more severe because, in addition to the local edema, laryngeal edema can occur, with blockage of the upper airways. The trunk has vital organs such as the heart and lungs, as well as vessels of great caliber and high pressure that contribute to the dispersion of venom through the body¹³.

Approximately 47% of cases received medical care within 3 hours of the incident. This mean interval until medical care is also observed in epidemiological studies involving accidents with venomous animals 14,19 . Most moderate/severe accidents were treated within 1 hour, indicating that the search for medical care in these cases was higher. In addition, these findings show that the health service from the state of Rio Grande do Norte was efficient in the face of emergency cases. Most cases were mild and progressed to cure, confirming the positive prognosis reported by other authors 12,19,24,26 . However, since underreporting is a reality in Brazil 26 , the low number of severe cases (n = 3) may not represent the real magnitude of the incidents. Despite the low number of deaths, the accident with bees is still a concern, as it may often be a case of a medical emergency. Also, since antivenom is undergoing clinical trials, severe cases have only been treated with clinical support 27,28 .

Local manifestations were more frequent (n = 1,893; 91%). Pain (86,6%) and edema (82.2%) were the most frequent local symptoms. In 9% of cases, the victims manifested systemic symptoms, such as headache, vagal manifestations, dyspnea, fever, and neuroparalytic

manifestations. Linard et al. and Diniz et al. also reported these local and systemic manifestations. These authors showed that local manifestations such as pain and edema ranged from 89 to 92% and 64 to 81%, respectively, while systemic manifestations varied from 6.5 to 12%^{12,24}. The presence of systemic manifestations is associated with cases of greater severity (χ^2 test between systemic manifestations and severity: p = 0.000, OR = 6.7, 95%CI 4.294 – 10.350). Cases with systemic manifestations are about seven times more likely to be moderate or severe. The age of the victim and the interval between the sting and medical care are not related to systemic manifestations. However, they are associated with severity. Due to the strong association between systemic manifestation and severity, the variables age and interval between the sting and medical care might also be related to systemic manifestation. This difference may have been due to the failure in completing the notification forms. It is possible that, when filling the information, the team recorded the severity of the case but not the systemic manifestation presented by the victim. Due to the high incidence of bee accidents, more regional epidemiological studies of this nature are necessary, since underreporting is still high, which makes it difficult to know the real dimension of the envenomation by honeybee at a local and/or regional level. The improvement of public health actions requires the training of health professionals responsible for treating victims and reporting cases.

CONCLUSIONS

Honeybee sting cases in Rio Grande do Norte have a high incidence in all locations of the state, especially in semi-arid regions. The economically active population is the most affected by accidents, but moderate/severe cases predominate among individuals over 60 years of age. Cases were reported in all months of the analyzed years and occurred mainly in urban areas and among men. Nevertheless, the most severe cases were reported in rural areas. The most common anatomical sting sites were the head and the hand, but severe cases were more frequent among victims stung in the head and trunk. Most victims received medical care within 1 hour after the incident. The majority of cases were mild and progressed to cure. Local manifestations were more frequent than systemic ones. Pain and edema at the sting site were the most common local symptoms. The high number of bee stings reveals that Rio Grande do Norte may be an important risk area for this type of injury, which needs to be monitored and controlled throughout the year.

ACKNOWLEDGMENTS

We thank the workers of the Health Department of the state of Rio Grande do Norte for kindly providing us with the epidemiological data.

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Received on: 05/17/2018 Revised on: 09/05/2018 Accepted on: 11/09/2018

Authors' contribution: Michael Radan de Vasconcelos Marques: writing, statistical analysis, results, and discussion; Kaliany Adja Medeiros de Araújo: map production and statistical analysis; Aluska Vieira Tavares: discussion; Alecxandro Alves Vieira: statistical analysis and statistical review; Renner de Souza Leite: introduction and general review.