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ORIGINAL RESEARCH

Toxicology

Epidemiology and characteristics of coral snake bites reported to the National Poison Data System (2006–2022)

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Abstract

Objectives: North American coral snake envenomations can result in life-threatening neurotoxicity. Their bites are relatively rare, making large studies difficult. Using the National Poison Data System (NPDS), we sought to investigate the epidemiological trends and clinical outcomes associated with North American coral snake bites over a 17-year period.

Methods: NPDS cases involving coral snakes from January 1, 2006, to December 31, 2022, were analyzed. Data collected included patient age, date, geographic location, clinical effects, treatments administered, and medical outcomes including incidence of “dry bites” (non-envenomation) and death.

Results: During the 17-year period, a total of 1374 cases were reported and analyzed. Cases included adults (≥ 20 years), accounting for 80% ($n = 1107$), and pediatric patients (≤ 19 years), accounting for 20% ($n = 267$) of total cases. Out of 50 US states and District of Columbia, 20 states reported cases. Florida and Texas accounted for 90.5% of all bites ($n = 1243$) with April being the month with the most reported cases ($n = 184$). The most bites ($n = 96$) were reported in 2008 and the fewest ($n = 69$) in 2016. Male patients predominated for both pediatric (75.7%, $n = 202$) and adult cases (75.3%, $n = 834$). Moderate to major clinical outcomes were documented in approximately 30% of total cases; with no reported deaths. Moderate effect is defined as the patient exhibited symptoms as a result of the exposure that were more pronounced, more prolonged, or more of a systemic nature than minor symptoms. Major effect was defined as the patient exhibited symptoms as a result of the exposure that were life threatening or resulted in significant residual disability or disfigurement. The three most reported clinical effects were wound/sting, dermal irritation/pain, and edema. Antivenom was administered in 21% ($n = 286$) of total cases and 37% ($n = 511$) of patients were admitted to a critical care unit. Dry bites occurred in 7% ($n = 100$) of total cases.

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Conclusion: Coral snake bites were rare, but consistently reported. While bites were associated with significant morbidity in adult and pediatric patients, there were no deaths reported. Antivenom use declined over the study period but was not associated with an increase in morbidity. An increased incidence of intubations was seen in association with decreased antivenom use.

KEYWORDS

antivenom, coral snake, elapidae

1 | INTRODUCTION

1.1 | Background

Worldwide, venomous snake bites represent a significant yet often overlooked public health issue, with millions of bites resulting in estimates of 100,000 or more deaths per year.¹ In the United States, the burden of venomous snake bites is far less but still significant with prior studies suggesting less than 5000 cases per year.² North American coral snake bites account for only a small fraction of this total, with less than 100 cases annually.² North American coral snakes belong to the Elapidae family and three species are found in the United States: *Micrurus fulvius* (eastern coral snake), located in Florida and the southeast United States, *Micrurus tener* (Texas coral snake), located in Texas and northwestern Mexico, and *Micruroides euryxanthus* (Sonoran coral snake), located in the southeastern United States and the state of Sonora, Mexico.³ All North American coral snakes have a red–yellow–black color pattern and possess small fixed front fangs.³

1.2 | Importance

Current medical literature on North American coral snake bites is limited and analysis of a national database, such as the National Poison Data System (NPDS), which is the data repository for the 55 poison control centers (PCC) in the United States, would allow for better understanding of management and clinical outcomes of North American coral snake bites. Despite relatively low incidence of venomous bite occurrence, North American coral snake envenomations have the potential to cause life-threatening complications, particularly respiratory muscle weakness and may require antivenom therapy, mechanical ventilation, and critical care.^{4,5} Thus, coral snake envenomations are an example of a high risk and low prevalence disease.

1.3 | Goals of this investigation

We sought to investigate the epidemiological trends and clinical outcomes associated with North American coral snake bites as reported to the NPDS from 2006 to 2022.

2 | METHODS

2.1 | Study design and setting

This study was approved by the America's Poison Centers' (APC's) Board of Directors. The NPDS was queried for all human exposures involving a reported bite from a coral snake that occurred between January 1, 2006, and December 31, 2022.

2.2 | Data source

NPDS is the data repository for the 55 PCC in the United States. These 55 centers service and collect data from all 50 states, District of Columbia, Puerto Rico, the Federated States of Micronesia, American Samoa, the US Virgin Islands, and Guam. Calls regarding potential poison exposures, including snake bites, are received by these poison centers. Certified specialists in poison information (CSPIs) gather detailed demographic and clinical information about the incident including medical outcomes. CSPIs then use a standardized coding system to assign a specific generic code to the exposure. In this regard, coral snake bites have a unique identifier within the NPDS data repository. These cases are then deidentified and uploaded to the NPDS. For research purposes, the NPDS data based can be queried for cases identified by the specific coral snake bite code and these cases are deidentified and extracted from the database for analysis.

2.3 | Selection of subjects

All cases entered in to the NPDS between January 1, 2006, and December 31, 2022, with the coral snake unique identifier were identified. All associated data from the identified cases were extracted into a Microsoft Excel file for analysis.

2.4 | Outcomes

Medical outcomes were defined as per the NPDS Coding Users' Manual (version 4.1), including no effect, minor effect, moderate effect, major effect, and death. These are standard definitions which are not

specific to snake bites. *No effect* was defined as the patient developed no symptoms as a result of the exposure. *Minor effect* was defined as the patient exhibited some symptoms as a result of the exposure, but they were minimally bothersome to the patient and the patient returned to a pre-exposure state of well-being with no residual disability or disfigurement. *Moderate effect* is defined as the patient exhibited symptoms as a result of the exposure that were more pronounced, more prolonged, or more of a systemic nature than minor symptoms; usually some form of treatment was or would have been indicated, but the symptoms were not life threatening, and the patient returned to a pre-exposure state of well-being with no residual disability or disfigurement. *Major effect* was defined as the patient exhibited symptoms as a result of the exposure that were life threatening or resulted in significant residual disability or disfigurement. *Death* was defined as the patient died as a result of the exposure or as a direct complication of the exposure where the complication was unlikely to have occurred had the toxic exposure not preceded the complication. In this study, any reported exposure that resulted in no medical effect was designated a non-envenomation bite or “dry bite.” This is consistent with prior published study definitions.²

Pertinent and common clinical effects and medical therapies were documented. Clinical effects with specific definitions per the NPDS Coding User’s Manual (version 4.1) included: rhabdomyolysis—the presence of myoglobin in the urine or a creatine kinase level >500 IU/L, low platelets—platelet concentration <150,000/μL, hypotension—blood pressure <90 mmHg systolic or >15 mmHg less than patient’s usual systolic blood pressure, and respiratory depression—respiratory rate <10 breaths/min or apply age-related standards for children and/or a SpO₂ ≤90%.

By NPDS definition, a pediatric patient is 19 years old or less.

2.5 | Data analysis

All available data were analyzed using SPSS for Macintosh (version 25.0; IBM SPSS Statistics). For this study, a total of 1107 adult cases and 267 pediatric cases were followed to a known outcome and were included for analysis. As this was a retrospective, descriptive study, no statistical analysis was performed.

3 | RESULTS

3.1 | Demographic trends

Over the 17-year study period, there were 1374 cases reported to the NPDS involving suspected bites by North American coral snakes, which were followed to a known medical outcome. Of these, 267 (19.4%) involved pediatric cases versus 1107 (80.6%) adult cases. Average age for pediatric cases was 13.0 years (standard deviation [SD] 5.25) and 43.8 years (SD 15.06) for adult cases. Male patients predominated for both pediatric (75.7%, $n = 202$) and adult cases (75.3%, $n = 834$).

The Bottom Line

Despite low incidence of venomous bite occurrence, North American coral snake envenomations have the potential to cause life-threatening complications. We sought to investigate the epidemiological trends and clinical outcomes associated with North American coral snake bites as reported to the National Poison Data System from 2006 to 2022. Of the 1374 reported cases, moderate or major medical outcomes were seen in 28%, and 35% were admitted to a critical care unit. Antivenom use declined over the study period but was not associated with an increase in morbidity. An increased incidence of intubations were seen in association with decreased antivenom use.

3.2 | Time-based trends

The year with the most total cases reported was 2008 with 96 cases while 2016 had the fewest cases reported at 69 cases. Figure 1 demonstrates the yearly trends in cases by age group. April was the month with the most reported total cases ($n = 184$) and pediatric cases ($n = 46$). September had the most adult bites reported ($n = 151$). Figure 2 demonstrates the number of cases by month and age group.

3.3 | Geographical trends

The state with the most reported bites was Florida with 671. Two states, Florida and Texas accounted for 90.5% of all bites with 1243 bites. Cases were reported from 20 states. Among these were 11 states where coral snakes are not endemic, including California ($n = 4$), New York ($n = 5$), and Michigan ($n = 3$). Figure 3 demonstrates the total number of cases reported from each state over the study period.

3.4 | Clinical outcomes and trends

Major or moderate clinical outcomes were documented in 29.6% ($n = 79$) of pediatric cases and 28% ($n = 311$) of adult cases. No deaths were reported in either age group.

Among all cases, the most common clinical effects reported were wound/sting ($n = 1374$), dermal irritation/pain ($n = 775$), and edema ($n = 575$). Multiple neurological symptoms were reported, with numbness ($n = 174$) and muscle weakness ($n = 33$) being the most common. Table 1 lists common and pertinent clinical effects reported in adult and pediatric cases, respectively.

A total of 44.6% ($n = 119$) of pediatric cases and 35.4% ($n = 392$) of adult cases were admitted to a critical care unit (CCU). Overall, 56.2% ($n = 150$) of pediatric cases and 47.4% ($n = 525$) of adult cases were admitted to a healthcare facility. Table 2 lists medical outcomes,

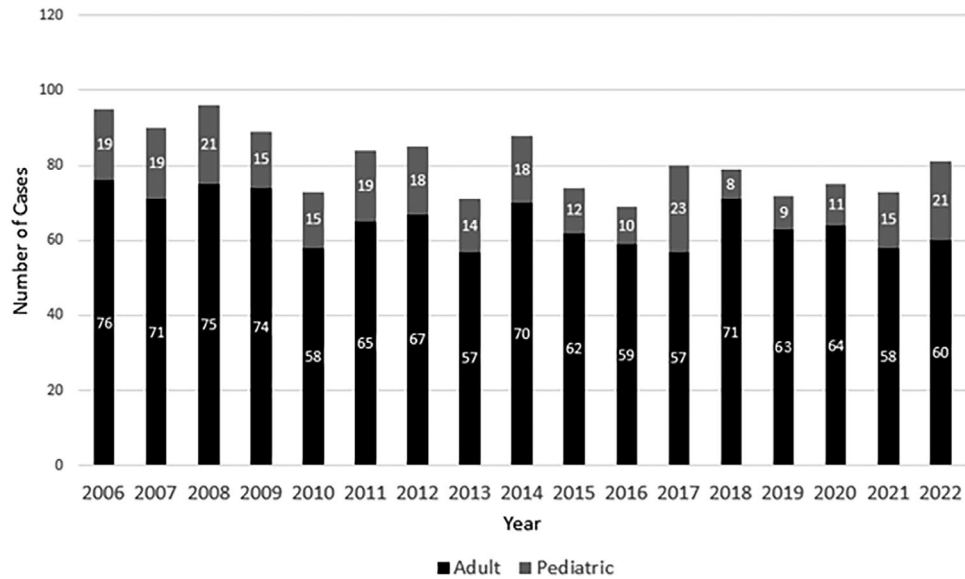


FIGURE 1 Coral snake bites by age group and year reported to National Poison Data System (NPDS) from 2006 to 2022.

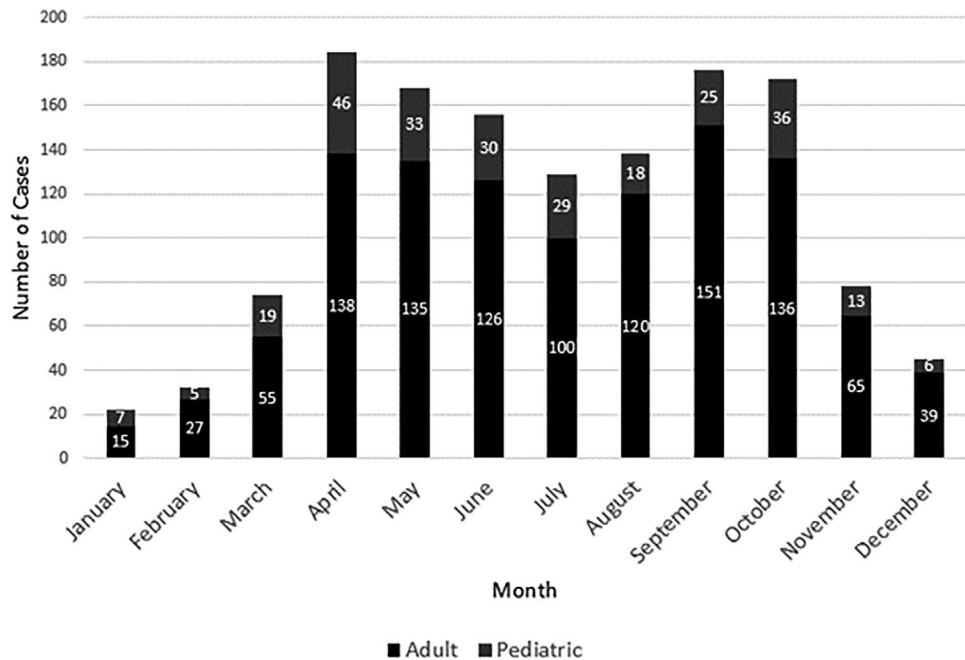


FIGURE 2 Coral snake bites by age group and month reported to National Poison Data System (NPDS) from 2006 to 2022.

disposition, and treatments rendered by age group. Dry bites occurred in 10.1% ($n = 27$) of pediatric bites compared to 6.6% ($n = 73$) of adult bites. The number of dry bites reported per year is shown in Figure 5.

3.5 | Treatment trends

Antivenom was administered in 63 pediatric (23.6%) and 223 adult cases (20.1%) over the study period. In 2006, antivenom was docu-

mented as being given 39 times. This was the peak year for antivenom administration. The years of 2016 and 2017 saw the fewest cases of antivenom administration with seven and eight cases, respectively. Figure 4 shows the yearly trend in antivenom administration by age group in relation to intubation rates and critical care admissions. Overall, 33% ($n = 95$) of total antivenom administration occurred in the first 3 years of this study for an average of 32 administrations per year versus an average of 14 administrations per year for the remaining 14 years. This decline in antivenom administration was neither associated

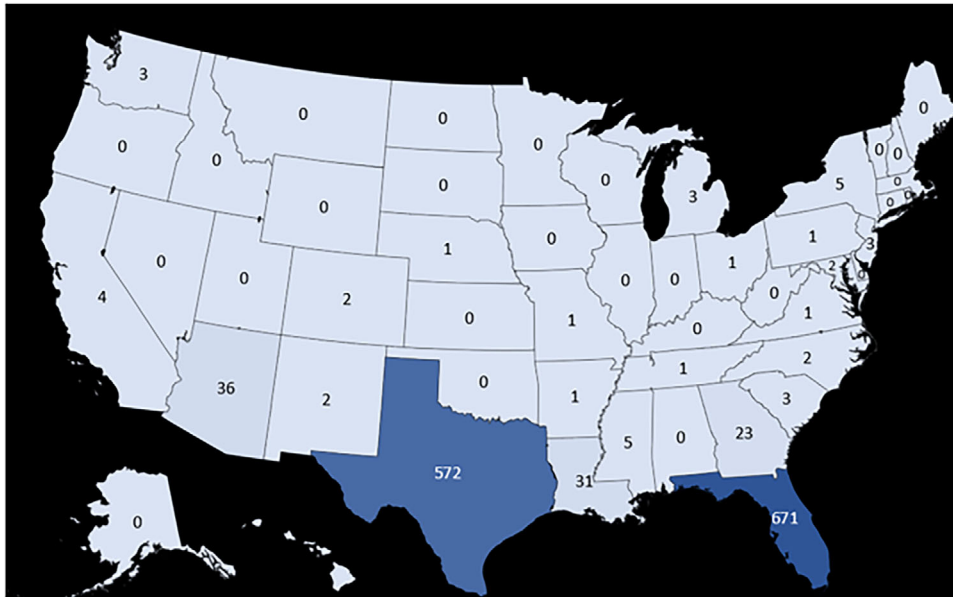


FIGURE 3 Coral snake bites reported to the National Poison Data System (NPDS) by state from 2006 to 2022.

with an increase in mortality nor in critical care admissions for either adult or pediatric patients. From 2006 to 2008, 38.3% ($n = 60$, 95% confidence interval [CI]: 26.1–51.8) of pediatric cases were admitted to a critical care setting compared to 46.4% ($n = 96$, 95% CI: 39.4–53.4) in 2009–2022. Of the adult cases, 37.8% ($n = 84$, 95% CI: 31.4–44.6) were admitted to a critical care setting in 2006–2008 compared to 40.7% ($n = 308$, 95% CI: 37.2–44.3) over the 2009–2022 time period. However, there was an increase in intubations after 2008. No cases of intubation were reported in the pediatric or adult groups before 2008 but subsequently, 0 pediatric cases and 16 adult cases of intubation were reported between 2009 and 2022.

4 | LIMITATIONS

Multiple limitations exist for this study. This was an analysis of an existing dataset of reported cases from regional poison centers. Therefore, reporting bias is possible and this dataset may not capture the full set of coral snake bite cases across the United States, including cases not reported or treated at PCC. The nature of the NPDS also minimizes the level of detail of the data limiting conclusions that can be drawn from it. Specific to this limitation is that there is no independent confirmation of the species of snake involved in a vast majority of cases. Snake species is typically based on the patient's description or report. This could result in misattributing other snake bites for coral snake bites or vice versa. The number of dry bites could be falsely elevated if the patient was actually bit by a non-venomous snake and misidentified the culprit. There are a few instances that bites were reported in non-endemic areas which may have resulted in incorrect geographic documentation. Geographic location of where the bite occurred may be incorrect due to call routing or reporting errors. An additional reporting bias is that people may not communicate bites unless they

experienced notable symptoms. As a result, documentation for the range of clinical effects and interventions may be curtailed. Since North American coral snakes bite cases are relatively rare, this smaller number of reported bites may also result in higher rates of chance findings and affect generalizability of treatments and outcomes.

The APC maintains the NPDS; it houses de-identified case records of self-reported information collected from callers during exposure management and poison information, which is controlled by the country's 55 regional PCC. NPDS data do not reflect the entire universe of exposures to a particular substance as additional exposures may go unreported to PCC. Accordingly, NPDS data should not be construed as representing the complete incidence of United States exposures to any substance(s). Exposures do not necessarily represent poisoning or overdose and APC is not able to completely verify the accuracy of every report. Findings based on NPDS data do not necessarily reflect the opinions of the APC.

5 | DISCUSSION

This is the largest study of North American coral snake bites in the medical literature. Prior publications were primarily case reports or series with geographical or chronological limitations.^{6–9} For instance, several studies have focused on Texas coral snake, while others included only Eastern coral snake exposures.^{6–9} The largest previously published study of 399 cases included all three North American coral snake species covering 5 years.²

The number of annual coral snake bites appear to be remarkably steady, with Seifert et al. reporting an average of 80 coral snake bites per year which is consistent with our findings.² This contrasts with crocotalid bites, which studies have shown 100% increase in events reported for some species over the last 10 years.¹⁰

TABLE 1 Common and pertinent clinical effects by age group reported to the National Poison Data System (NPDS) from 2006 to 2022.

Clinical effects (%)	Adult	Pediatric
Tissue effects		
Wound/sting	100% (n = 1107)	100% (n = 267)
Dermal irritation/pain	56.3% (n = 623)	56.9% (n = 152)
Edema	39.1% (n = 433)	53.2% (n = 142)
Ecchymosis	5.2% (n = 58)	1.9% (n = 5)
Necrosis	0% (n = 0)	0% (n = 0)
Rash	1.7% (n = 19)	2.2% (n = 6)
Hematological effects		
Hemolysis	0% (n = 0)	0% (n = 0)
Coagulopathy	<1% (n = 1)	0% (n = 0)
Rhabdomyolysis	<1% (n = 1)	0% (n = 0)
Low platelets	0% (n = 0)	0% (n = 0)
Neurological effects		
Muscle weakness	2.5% (n = 28)	1.9% (n = 5)
Numbness	13.1% (n = 145)	10.9% (n = 29)
Paralysis	<1% (n = 9)	0% (n = 0)
Fasciculations	<1% (n = 5)	<1% (n = 1)
Myoclonus	0% (n = 0)	0% (n = 0)
Tremor	<1% (n = 7)	0% (n = 0)
Peripheral neuropathy	1.6% (n = 18)	1.1% (n = 3)
Other neurological	1.2% (n = 13)	1.5% (n = 4)
Other effects		
Hypotension	<1% (n = 9)	<1% (n = 1)
Nausea/vomiting	8.7% (n = 96)	13.1% (n = 35)
Respiratory depression	<1% (n = 7)	1.1% (n = 3)

TABLE 2 Medical outcomes, disposition, and treatments rendered by age group.

	Adult	Pediatric
Clinical outcomes (%)		
Minor effect	43.8% (n = 485)	47.9% (n = 128)
Moderate effect	25% (n = 277)	27.3% (n = 73)
Major effect	3.1% (n = 34)	2.2% (n = 6)
Death	0% (n = 0)	0% (n = 0)
Admitted to non-critical care unit	12% (n = 133)	11.6% (n = 31)
Admitted to critical care unit	35.4% (n = 392)	44.6% (n = 119)
Therapies (%)		
Antivenom	20.1% (n = 223)	23.6% (n = 63)
Intubation	1.4% (n = 16)	0% (n = 0)
Vasopressors	<1% (n = 3)	1.1% (n = 3)
Antibiotics	5.3% (n = 59)	3.45% (n = 9)
Opioid analgesics	37.9% (n = 42)	4.9% (n = 13)

Although 20 states reported coral snake bites, most of the cases reported occurred in the states of Texas and Florida ($n = 572$ and 671 , respectively), comprising 90% of bites. This was an expected finding given the range of the Texas and Eastern coral snake and the large human populations of Texas and Florida. Arizona was the state with the third highest bites reported ($n = 36$) likely due to the presence of the Sonoran coral snake, whose bites, due to their small size, are not usually considered medically significant. Of note, there were no bites reported from the state of Alabama where the Eastern coral snake is found. The reasoning behind this lack of reported bites is unclear but is consistent with prior studies.² It is also notable that coral snake bites were reported from multiple states where coral snakes are not endemic. In all, 13 non-endemic states reported coral snake bites during the study period. There are several possible explanations of these non-endemic reports such as "out of state" calls from endemic states being incorrectly routed and documented in non-endemic states or simple errors in location documentation.

Most coral snake bites in this study occurred in the spring and fall, with a slight decline seen in July and August. This contrasts with the Seifert et al. study, which reported the most bites occurring in July.² In the present study, 82% of bites occurred between the months of April and October with an expected decline in number of bites during cooler months when coral snakes are presumed to be less active and less human activity may occur due to the weather.

While coral snake bites are uncommon, they represent a clinically concerning event as they can result in serious adverse outcomes.^{4,5} In particular, there is the risk of paralysis and respiratory failure due to the neurotoxic nature of the venom leading to death.^{4,5} Coral snake venom contains a mixture of proteins, specifically phospholipases A2 (PLA2) and "three-finger" toxins, which are thought to contribute to its neurotoxic properties.¹¹ Inhibition of postsynaptic nicotinic acetylcholine receptors at the neuromuscular junction, can cause motor weakness and paralysis.¹²

However, in the present study, neurological symptoms were uncommon. Numbness was the most common neurological symptom, seen in approximately 13% of adult cases while paralysis occurred in less than 1% of adult cases. Local symptoms, such as pain and edema, predominated. This is consistent with other studies which have found pain or edema to be the most commonly reported symptoms.^{2,6,8} Despite the lack of serious neurological symptoms, suspected coral snake bites still resulted in serious outcomes with approximately 28% of patients having either a major or moderate clinical outcome and over 35% admitted to a CCU. Rates of intubation and mechanical ventilation were low and no deaths were reported in this study. However, a death from a coral snake bite was published during the study time period but apparently was not reported to a PCC.⁵

There are reports of up to 30% or more of venomous snake bites resulting in dry bites.¹³ Our study had a lower dry bite rate of 7.3%. This is lower than other coral snake studies have reported. A study of 39 reported Eastern coral snake bites found a 25% dry bite rate, while Seifert et al reported a 10% dry bite rate in coral snake cases.^{2,9} It should be noted that the lower dry bite rate seen in the present study remains higher than the 1%–6% reported with crotalid bites.^{2,10}

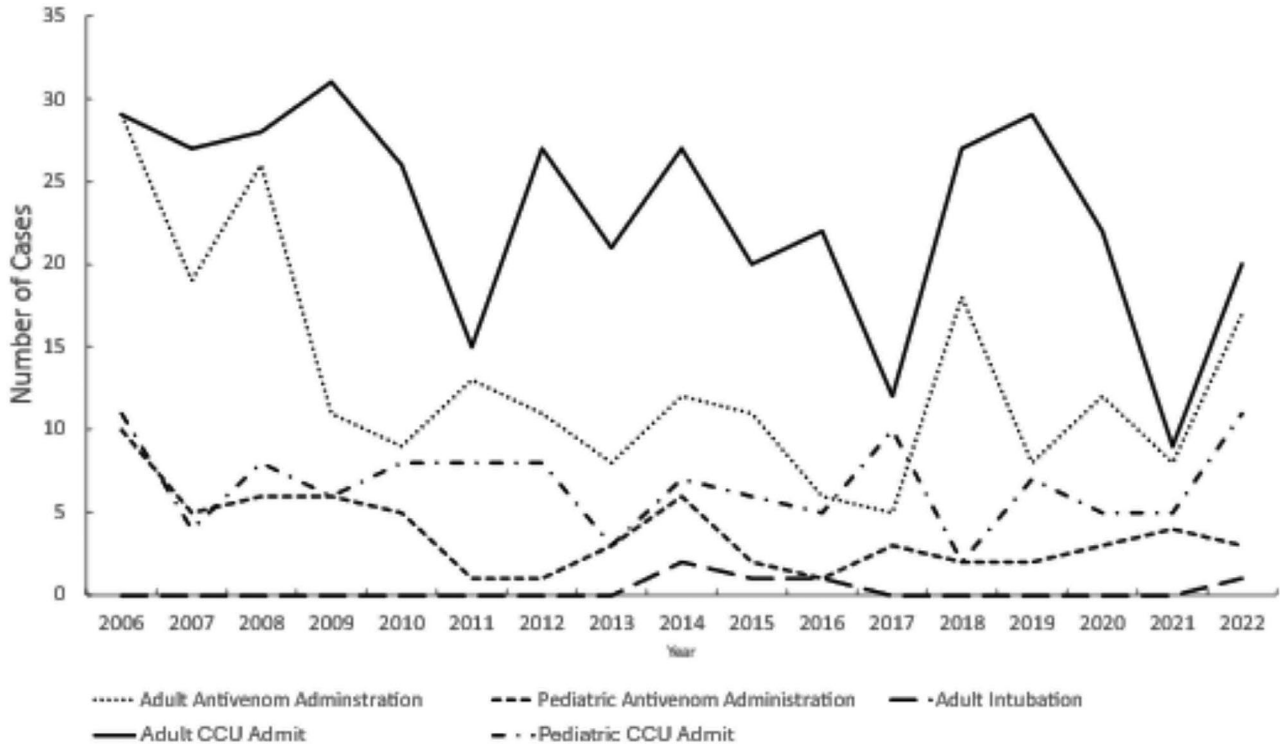


FIGURE 4 Antivenom administration, intubation, and critical care unit (CCU) admission by age group and year reported to the National Poison Data System (NPDS) from 2006 to 2022.

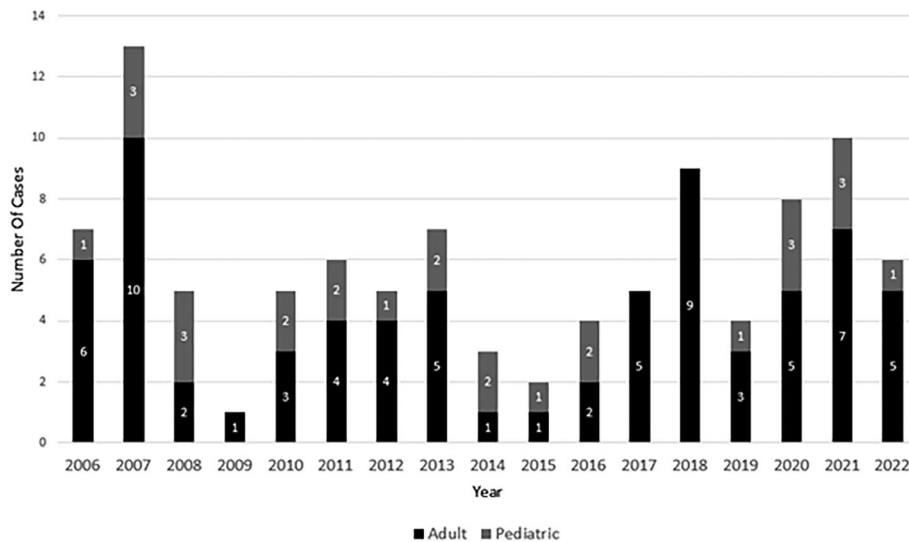


FIGURE 5 Number of dry bites reported by age group reported to the National Poison Data System (NPDS) from 2006 to 2022.

In this study, antivenom was administered in 21% of cases ($n = 286$). This is significantly less compared to the study by Seifert et al., which demonstrated a 46% ($n = 182$) antivenom administration rate.² The explanation for this decline may be due to lack of availability of the antivenom. In the United States, there is only one Federal Drug Administration (FDA) approved coral snake antivenom, the North American Coral Snake Antivenin, which is a sheep derived whole immunoglobulin G (IgG) product effective against both the Texas and Eastern coral snake.¹⁴ However, this antivenom has not been commercially produced

since 2006 and all lots expired in 2008. The FDA has subsequently extended the expiration date of remaining lots of the antivenom, with the most recent extension until June 20, 2024, but the number of available doses continues to decrease with usage.¹⁵ The fact that in the present study 33% ($n = 95$) of all antivenom administration occurred between 2006 and 2008 is consistent with a decrease in availability driving reduction in antivenom usage. Fortunately, this reduction in antivenom administration was not associated with increased mortality or critical care admissions in our study but was associated with

more cases of intubation. The number of vials of North America coral snake antivenom administered was not recorded in the present study; however, the package insert recommends 3–5 vials; some studies suggest up to 10 vials may be needed.^{14,16} Similarly, complications from antivenom administration were not recorded in this study, but as with any whole IgG product, development of anaphylaxis and serum sickness would be a potential concern.¹⁴

In summary, from 2006 to 2022, NPDS documented a total 1374 coral snake bite cases in the United States that were followed to a known outcome. Overall, the number of annual cases remained stable from 2006 to 2022. The majority of cases were male and occurred during the spring and fall. Florida and Texas accounted for 90% of total cases but 20 other states reported bites. Moderate or major medical outcomes were seen in 28% of cases and 35% were admitted to a CCU. Antivenom use declined over the study period but was not associated with an increase in morbidity. An increased incidence of intubations were seen in association with decreased antivenom use. There were no deaths reported in this study.

AUTHOR CONTRIBUTIONS

Mary E. Velagapudi, Juliana J. Navarro, and Alexander E. Hill contributed to writing of the manuscript. Michael A. Darracq and Stephen L. Thornton contributed to hypothesis development and analysis of database. Stephen L. Thornton takes responsibility for the paper as a whole.

CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

FUNDING INFORMATION

The authors received no specific funding for this work.

DATA AVAILABILITY STATEMENT

All de-identified data files and data elements/definitions are available as of March 19, 2024, at the National Poison Data System repository at the following URL: <https://www.aapcc.org/national-poison-data-system>.

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