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Original Research

Population-based study of venomous snakebite in Taiwan

Chun-Kuei Chen [a,†], Chih-Chuan Lin [a,†], Fuh-Yuan Shih [b], Chung-Hsien Chaou [a], Jasper Chia-Cheng Lin [b], Ting-I Lai [b], Chiung-Yao Tseng [a], Cheng-Chung Fang [b,c,*]

[a] *Department of Emergency Medicine, Linkou Chang Gung Memorial Hospital, Chang Gung University, Taoyuan, Taiwan*
[b] *Department of Emergency Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan*
[c] *Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan*

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Abstract

Background: The epidemiological features of snakebite are fragmented and inadequate in most countries. The true impact of snakebite is also very likely to be underestimated, and reliable information on its incidence, morbidity, and mortality is limited worldwide.
Methods: We perform a nationwide epidemiological study of snakebite by extracting claim record data from Taiwan's National Health Insurance database to explore the epidemiology of venomous snakebite from years 2005 to 2009.
Results: A total of 4647 snakebites were reported in 2005–2009. The nationwide annual incidence of snakebite was 40.49 per million persons. Hemorrhagic-type snakebites (*Viridovipera stejnegeri* and *Protobothrops mucrosquamatus*) accounted for 71.78% of the cases, while neurotoxic-type snakebites (*Naja atra* and *Bungarus multicinctus*) accounted for 19.21%. Only a few cases of snakebites were caused by *Deinagkistrodon acutus* (0.73%). Although the east part of Taiwan accounted for only one-sixth of the total number of cases, the same area had the highest incidence of snakebite, about seven times the national incidence. Fifty-nine percent ($n = 2747$) of victims were between the age of 41 years and 70 years, and mostly in the age group of 51–60 years ($n = 1026$, 22%). The highest incidence (130.4 per million persons) was in the age group of 71–80 years. In general, snakebite victims suffered minor injuries. Overall, hospital admission was 35.8%, and only about 3.6% patients were needed to be admitted to the intensive care unit. During this study period, only two cases of mortality were documented.
Conclusion: In this population-based study, the annual incidence of venomous snakebite was 40 per million people. Cases of venomous snakebite are geographically unevenly distributed in Taiwan. Due to effective antivenom therapy, the outcome of the snakebite patients was favorable.

Keywords: antivenom; epidemiology; snakebites

1. Introduction

There are very few wide-scaled epidemiological studies of snakebite. The true impact of snakebite is often underestimated, and trustworthy information on incidence, morbidity, and mortality is inadequate worldwide.[1,2] Population-based studies of incidence and mortality from snakebite are currently lacking and are urgently needed to investigate the full scale of the disease.[3] A Pacific subtropical island with mountains and forests, Taiwan is an ideal habitat for several species of snakes. However, similar to its neighboring tropical countries, a nationwide epidemiological study on snake envenomation is lacking. Epidemiological studies of snakebite in Taiwan were mostly conducted in a single hospital setting.[4] Therefore, it is very difficult to make conclusions pertaining to the need of antivenoms nationwide, the efficacy of such a therapy, and the scale of progress made on snakebite treatments.[5]

* Corresponding author. Department of Emergency Medicine, National Taiwan University Hospital, Number 7, Chung-Shan South Road, Taipei 100, Taiwan.
E-mail address: conrad@ntu.edu.tw (C.-C. Fang).
† These authors contributed equally to this article.

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There are six species of snakes throughout Taiwan that release deadly toxins, which can result in life-threatening complications. The four species of snakes in Taiwan that secrete hemorrhagic venom are *Viridovipera stejnegeri* (formerly *Trimeresurus stejnegeri*, Taiwan bamboo viper or green habu), *Protobothrops mucrosquamatus* (formerly *Trimeresurus mucrosquamatus,* Taiwan habu), *Deinagkistrodon acutus* (hundred-pacer), and *Daboia russelii siamensis*. These venoms cause local tissue swelling that can progress to severe compartment syndrome on the limb where venom was injected. In patients with severe tissue swelling, surgical intervention such as debridement, fasciotomy, or graft may be needed. Snakes releasing neurotoxic venoms are *Naja atra* (Chinese or Taiwan cobra) and *Bungarus multicinctus* (Taiwan banded krait). These venoms can cause respiratory distress due to muscle paralysis and other neurological manifestations such as diplopia, dysarthria, and extremity paralysis. Between the two species, *B. multicinctus* venoms result in a more profound neurological deficit than the venoms of *N. atra*. However, *N. atra* venoms can result in tissue damages as well as neurological deficits. Surgical intervention such as debridement, fasciotomy, or skin graft may also be needed in the treatment of *N. atra* snakebite.

In the 1960s, Taiwan began to develop antivenoms for some venomous snake species, but only about 15% of the cases were given antivenoms. At that time, most cases of snakebites were treated with herbal medicine instead.[6] In 1980s, the $F(ab')_2$ of horse immunoglobulin G antivenoms were developed by the Vaccine Center, Center for Disease Control, Taipei, Taiwan.[7–9] At present, four antivenom regimens are available in the country. The bivalent antivenom FH is effective against *V. stejnegeri* and *P. mucrosquamatus*, and another bivalent antivenom FN is effective against *B. multicinctus* and *N. atra*. The antivenom FA is effective against *D. acutus*. The antivenom FDrs that is effective against *D. russelii siamensis* was not developed until mid-2008.

Taiwan launched a single-payer National Health Insurance (NHI) program on March 1, 1995. According to the Bureau of NHI, the coverage of NHI has surpassed 96% of the national population, whereas the number of cooperating medical facilities has reached 95% in 2009.[10,11] The NHI database contains registration files and original claim data for reimbursement. After scrambling patients' identities, the database is provided to scientists in Taiwan for research purposes. With its nationwide coverage, it is pertinent for epidemiological studies and has been used widely in academic studies.[12] The purpose of this study was to perform a nationwide epidemiological study of venomous snakebite from 2005 to 2009. We intended to estimate the comprehensive epidemiological features of snake envenomation.

2. Materials and methods

2.1. Ethics statement

This study was approved by the Chang Gung Memorial Hospital Research Ethical Committee, Taoyuan, Taiwan (100−3049B). The identification of each patient was previously scrambled by the NIH Bureau; therefore, no informed consent was needed.

2.2. Data source and study methods

We used NHI claim data in the period of 2005−2009 for descriptive epidemiology studies. This data set included complete outpatient visits, hospital admissions, disease diagnosis, prescriptions, procedures, interventions, and vital statuses for the whole insured population. We established the longitudinal medical history of each beneficiary by linking several computerized administrative claim data sets to track the outcomes of the snakebite episodes. In the NHI database, each drug has its own drug code. By tracing the antivenom drug codes (drug codes J000006212 for FH, J000009212 for FN, and J000010209 for FA), we are able to retrieve cases treated by these antivenoms. As FDrs antivenom was not available prior to mid-2008, the cases that used FDrs antivenom were not included in this study. Patients who received only one type of antivenom for treatment were classified as FH group, FN group, or FA group, depending on the type of antivenom received. Patients who received more than one type of antivenom in a single episode of snakebite were classified as the mixed group.

Variables were extracted from the NHI database for descriptive and analytic epidemiological studies. Recorded variables were the following: patient's age, gender, the month of attack, and the location of the treating hospital. In the NHI system, Taiwan Island is divided into six districts: District 1 (the Taipei district), District 2 (the North district), District 3 (the Central district), District 4 (the South district), District 5 (the Kaohsiung district), and District 6 (the East district).

3. Results

A total of 4647 snakebite cases were reported in 2005−2009. There were 3340 (71.87%) episodes in the FH group, 893 (19.21%) in the FN group, 380 (8.10%) in the mixed group, and only 34 (0.73%) in the FA group. Most antivenom regimens used in the mixed group were the combination of FH and FN. The nationwide annual incidence of venomous snakebite was 40.49 per million persons (Table 1). The national annual incidence of the FH group was 29.10 per million persons, FN group was 7.78 per million persons, FA group was 0.30 per million persons, and mixed group was 3.31 per million persons. The geographic district incidences of snakebite are shown in Table 1 and Figure 1. District 1 had the highest case number. However, the incidence rate in District 1 was slightly less than the national incidence rate due to District 1 being the most densely populated area in the country. Although District 6 accounted for only one-sixth of the total cases, it had the highest incidence rate (about 7 times the national incidence rate). Regardless of the type of snakebite, District 6 had the highest incidence rate among all districts. District 3 had the lowest incidence of total snakebites but relatively high incidence rate in the FN group. FA group

Table 1
Case numbers and incidences (per million population) of snakebites in different regions of Taiwan during 2005–2009.

District	FH		FN		FA		Mixed		Total	
	Case no.	Incidence	Case no.	Incidence	Case no.	Incidence	Case no.	Incidence	Case no.	Incidence
1	1099	30.22	81	2.23	7	0.19	96	2.64	1283	35.28
2	479	28.26	133	7.85	2	0.12	93	5.49	707	41.71
3	396	17.78	203	9.11	4	0.18	51	2.29	654	29.37
4	345	20.17	142	8.30	1	0.06	42	2.46	530	30.99
5	416	22.77	187	10.24	4	0.22	37	2.03	644	35.25
6	605	209.25	147	50.87	16	5.52	61	21.05	829	286.70
Total	3340	29.10	893	7.78	34	0.30	380	3.31	4647	40.49

FA = cases receiving antivenom FA regimen; FH = cases receiving antivenom FH regimen; FN = cases receiving antivenom FN regimen; Mixed = cases receiving more than one antivenom regimen.

victims were rare and scattered across the island, with half of the cases found in District 6.

The majority of the snakebite victims was male ($n = 3279$, 70.5%). The ratios between male and female were 2.28 for the FH, 3.09 for the FN, 4.66 for the FA, and 1.96 for the mixed groups. The average age of all snakebite victims was 40.5 years. The case numbers and incidences among different age groups are shown in Figure 2. Fifty-nine percent ($n = 2747$) of victims were in the age group of 41–70 years, and most cases were in the age group of 51–60 years ($n = 1026$, 22%, Figure 2). However, when the incidences of different age groups were calculated, the highest incidence (130.4 per million persons) was in the age group of 71–80 years (Figure 2). Throughout the years, 77% ($n = 3584$) of snakebite incidence occurred from April to November, with the peak being in August (Figure 3). Snakebites in the FH group were in plateau status from May to November, whereas the case numbers in the FN group presented peaks in August (Figure 3).

The overall outcome of snakebite victims was favorable. General ward admission rate was 35.8%, and only about 3.6% patients needed to be admitted to the intensive care unit. The FA group had the highest intensive care unit admission rate, and the FH group had the lowest. There were only two cases of mortality during the study period (Table 2).

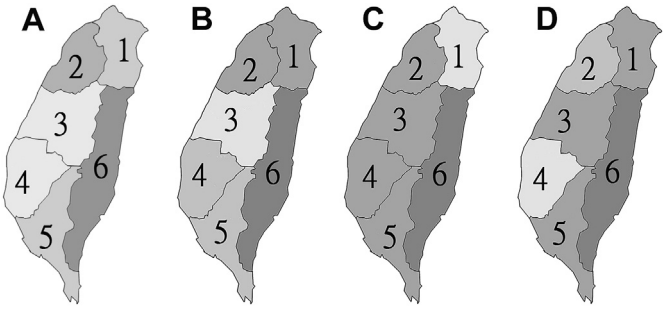

Figure 1. Incidences of snakebites in different regions of Taiwan in 2005–2009: (A) total venomous snakebites, and venomous snakebites in the (B) FH, (C) FN, and (D) FA groups. The darker the color, the higher the relative incidence in the region.

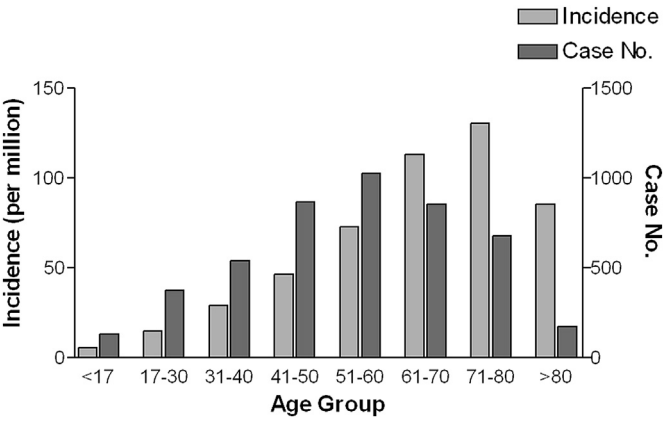

Figure 2. Age-wise distribution of snakebite victims in Taiwan during 2005–2009. Both the incidences and case numbers in different age groups are shown.

4. Discussion

4.1. Nationwide incidence and geographic differences of snakebites

In this study, a comprehensive epidemiological study of snakebite in Taiwan was demonstrated. This is the first nationwide population-based snakebite study in Taiwan, and to the best of our knowledge, there has been no nationwide

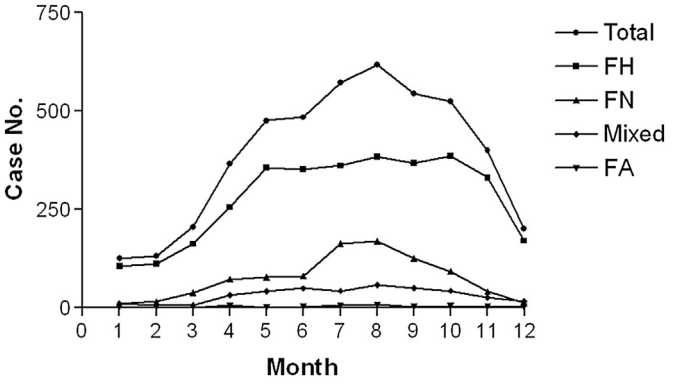

Figure 3. Month-wise distribution of snakebite incidences in Taiwan during 2005–2009. The case numbers in different months of the year are shown. FA = case numbers of the FA group; FH = case numbers of the FH group; FN = case numbers of the FN group; Mixed = case numbers of the mixed group; Total = overall case numbers.

Table 2
Outcome of snakebite patients in 2005–2009.

Group	Case no.	Ward	ICU	Death
FH	2644	837 (31.7)	42 (1.6)	0
FN	736	222 (30.2)	45 (6.1)	1 (0.1)
FA	28	12 (42.9)	4 (14.3)	0
Mixed	1239	591 (47.7)	78 (6.3)	1 (0.08)
Total	4647	1662 (35.8)	169 (3.6)	2 (0.04)

Data are presented as *n* (%) unless otherwise indicated.
FA = cases receiving antivenom FA regimen; FH = cases receiving antivenom FH regimen; FN = cases receiving antivenom FN regimen; ICU = admission to intensive care unit; Mixed = cases receiving more than one antivenom regimen; Ward = admission to general ward.

studies on the incidence of snakebite in today's literature.[3] Venomous snakebites were geographically unevenly distributed in Taiwan. The incidence rate in the east side of the island was about seven times the national incidence. This area of the island consists of mountains and forests, and is less populated. Our study reflected a need for any national health authority to acknowledge the geographic difference in dealing with snakebites, thus allocating medical resources accordingly. Another important finding discovered in this study was the age distribution of snakebite patients. The peak incidence, which was more than three times the national incidence, was in the age group of 71–80 years. The incidence in the age group of >81 years was more than two times the national incidence. This showed that the elderly people are most susceptible to snakebite in Taiwan. Snakebite prevention and education should be targeted to the elderly, especially those who live and work in rural areas.

Not only are snakes geographically distributed unevenly across the island, but also different species of snake become more active than others as time changes. The case numbers of snakebites differed in different regions and times, due to the different species of snakes and their population distribution. In this study, the FH group snakebite accounted for about 72% of the total cases, while the FN group accounted for 19%. In 1969, a survey on different snakebite groups was conducted throughout Taiwan. That report showed 558 cases in the FH group, 252 in the FN group, and 37 in the FA group.[6] The number of cases in the FN group decreased in our study compared to that of 40 years ago. Cases of snakebites caused by *D. acutus* were even fewer than those 40 years ago. This showed that throughout the years, the population of different species of snakes has changed.

4.2. Antivenom efficacy and safety

At present, the principal treatment of snakebite in Taiwan is antivenom therapy. Among the 4647 cases collected during the study period, there were only two cases of mortality. Forty years ago, the mortality rate from snakebite in Taiwan was about 1.4% when the use of antivenom therapy was uncommon.[6] This decrease in mortality rate showed the efficacy of antivenom treatment. As Taiwan is a part of Southeast Asia, many of its venomous snakes often have species under the same family inhabiting other countries in this region.[5] The low mortality rate from snakebite seen in Taiwan might be explained by the routine use of antivenom here.[3,5]

Sometimes, it is difficult to identify the species of the snake solely from the clinical presentation of the patient, especially when the snake was not available for identification. If the patient also failed to identify the culprit snake, then the correct diagnosis could be hard to achieve. Thus, in practice, different kinds of antivenoms may be administered to the patient. In our study, 380 (8.1%) cases received at least two types of antivenoms. The clinical presentations of different snakebites could be very similar. In some studies, these unidentified cases accounted for 12–45% of the total cases.[13–16] At the present time, there is a method of using blood assay to detect the *N. atra* venom, but it is not commercially available.[4] Other types of venoms cannot be identified by any laboratory test. Further research is needed to assure a correct diagnosis and improve the treatment.

4.3. Limitations

Using our database, we were unable to identify which snake species in the FH or FN group caused the snakebite. The incidence of snakebite could be underestimated due to neglected cases of dry bites, in which situation antivenom therapy would not be used. Due to the time of data collection, patients bitten by *D. russelii siamensis* were not included in this study. However, the number of cases in this category should be very small (the annual attacks ranged from 1 to 3).[4,6,15,17] Therefore, the underestimation of *D. russelii siamensis* attacks should have minimal influence on the epidemiology result of this study.

5. Conclusion

In this nationwide study, the annual incidence of venomous snakebite was 40 per million people. The geographic distribution of venomous snakebite is uneven in Taiwan. Due to an effective antivenom therapy, the outcome of the snakebite patients was favorable.

Conflicts of interest

None declared.

Acknowledgments

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