CLINICAL MANAGEMENT OF SNAKEBITES IN COMMUNITY CARE UNIT: A SINGLE-CENTER RETROSPECTIVE STUDY IN LOPBURI, CENTRAL THAILAND

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Abstract
Background: Snakebite, a neglected tropical disease, might result in severe clinical outcomes.
Objectives: This study presents a retrospective analysis of snakebite data from a community hospital in Lopburi, Central Thailand, and also assesses snakebite distribution and clinical management to lower mortality and morbidity in the community setting.
Methods: A cross-sectional retrospective study used data from October 1, 2014, to August 30, 2023, to determine the epidemiology, clinical profile, and management of snakebite patients who visited Pattananikom Hospital.
Results: The study included 225 snakebite patients with a median age of 39 (IQR 26-53 years), and 64.4% were male. The responsible species for half of the bite cases were unidentified (54.2%). Among 103 confirmed snakebites with identified species, there were 24 cobras (23.3%), 23 Russell's vipers (22.3%), 16 green pit vipers (15.5%), 4 Malayan pit vipers (3.9%), 2 Malayan kraits (1.9%), and 34 (33.0%) other nonvenomous snakes. Notably, 10 out of 24 patients (41.7%) encountering cobras were diagnosed with venom ophthalmia. For bites caused by unknown snakes, two patients experienced compartment syndrome, one had dyspnea, and one had ptosis. Thirteen patients, also bitten by unidentified snakes and eligible for antivenom, went untreated due to a shortage of polyvalent antivenom, resulting in referrals. From 2021 to 2023, 20 patients (55.6% of 36) were referred (p=0.026). Of the patients with thrombocytopenia, eight (57.1% of 14) were referred (p=0.001), as were all cases with systemic bleeding, dyspnea, ptosis, or compartment syndrome. Moreover, prophylactic antibiotics (amoxicillin-clavulanate) were routinely prescribed (82.7%).
Conclusion: Snakebites have been referred to more frequently in the last three years. Even though the origins of most cases are unknown and often lead to referrals, there is a notable shortage of polyvalent antivenoms. This scarcity has the potential to delay treatment and increase the risk of mortality. This study highlights the need for improved antivenom access in community hospitals to mitigate delays and reduce mortality.

Keywords: snakebite envenomation, epidemiology, clinical profile, snakebite management, antivenom availability, rural healthcare, Thailand

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Introduction

Snakebite envenomation is a severely neglected tropical disease. It primarily affects rural communities in low- and middle-income countries. The most impacted regions include Sub-Saharan Africa, South America, and South to Southeast Asia.[1, 2] It is estimated that around 5.8 million people are bitten by venomous snakes each year, causing 81,000 to 138,000 deaths annually, with Southeast Asia accounting for up to 70% of these cases.[3] This high prevalence is attributed to the region's suitable topography and climate for snakes and cultural practices such as farming and foraging that increase snake encounters.[3] In Thailand, the annual snake bite cases are estimated to be 8,525-8,906 cases per year, with 2 to 7 deaths and up to 7 amputations.[4] However, these numbers may be underestimated due to data limitations, particularly in remote areas with inadequate public health reporting.[5] This could be because victims may receive treatment from traditional healers, and some pass away before reaching hospitals.[6]

In Thailand, two groups of venomous snakes were classified based on the patient's clinical presentation following envenomation.[7] The neurotoxic snakes include cobra species (e.g., *Naja kaouthia* and *Naja sumatrana*), the King cobra (*Ophiophagus hannah*), Malayan krait (*Bungarus candidus*), and banded krait (*Bungarus fasciatus*). Their venom can cause muscle weakness, ptosis, slurred speech, difficulty in swallowing, respiratory distress, and potentially death from respiratory failure. The hematotoxic snakes include Russell's viper (*Daboia* spp.), Malayan pit viper (*Calloselasma rhodostoma*), and green pit viper species such as *Trimeresurus albolabris* and *Trimeresurus macrops*). Their venom affects the circulatory system and can cause disseminated intravascular coagulation (DIC), as the hematotoxin in the venom stimulates coagulation factors.[8] Certain snake venoms exhibit cytotoxic properties in addition to hepatotoxic and neurotoxic effects, which can result in tissue necrosis and the development of compartment syndrome.[9]

Early antivenom administration is needed when indicated. To prevent death and disability resulting from systemic and severe local snake envenoming. There are two types of antivenom: polyvalent, which targets multiple snake venoms, and monovalent, which is specific to a single snake species. Polyvalent antivenom is particularly valuable when the venomous snake species cannot be identified.[10] However, it is essential to administer antivenom only when indicated, as inappropriate use may provoke the risk of adverse reactions, ranging from mild symptoms such as urticaria and nausea to severe anaphylaxis.[11]

Although antivenom can significantly reduce morbidity and mortality in snakebite patients, access to effective antivenom administration remains inconsistent in some community hospitals in Thailand despite over 90% of cases having access to antivenom.[4, 12] To the best of our knowledge, there is limited data on the gaps in antivenom availability and its prevalence and impact among community hospitals. Moreover, many community hospitals often refer severe envenomation cases to higher-level hospitals due to limited capabilities and resources.[13]

These include the unavailability of specific monovalent or polyvalent antivenoms, the absence of mechanical ventilators, and the inability to provide comprehensive wound care. The referral process places a significant burden on community hospitals, requiring the involvement of at least one doctor, a registered nurse, and resources such as an ambulance and medical equipment.[13] This process can delay antivenom administration and contribute to increased mortality rates.[14]

Pattananikom Hospital, a community hospital in Lopburi, Central Thailand, serves as a primary care unit in a district with high fatal snakebite incidents. The hospital is responsible for treating individuals envenomed by snakes in such cases.[7, 8, 15] Given the limited data on the recent epidemiology of snakebites, this study examined the epidemiological profiles of snakebite patients using data from Pattananikom Hospital. Furthermore, this study aimed to analyze the clinical management of snakebite patients at Pattananikom Hospital and develop strategies to improve emergency care in community settings. This analysis would contribute to optimizing future strategies for managing resources and supplies in snake envenoming treatments.

Methods

Study Design and Subjects

This cross-sectional study was conducted at Pattananikom Hospital, Lopburi Province, Central Thailand. Secondary data were collected from snakebite patients' emergency department (ED) medical records between October 1, 2014, and August 30, 2023. A total of 225 snakebite cases were included in the study.

Data Collection

Data were extracted from the hospital's internal database, transferred into Excel, and reviewed using a standardized case record form for consistency and accuracy. The case record form included: (1) patient's characteristics such as age, gender, visit date, time of arrival at the ED, time of snakebite, bitten site, type of snake, and prehospital management;(2) laboratory tests performed at the ED before any treatment, including complete blood count (CBC), serum electrolytes, serum creatinine (Cr), 20-minute whole blood clotting time (20WBCT), venous clotting time (VCT), and international normalized ratio (INR), and follow-up values for 20WBCT and VCT recorded; and (3) management and outcomes, such as clinical manifestations, admission time, antivenom treatment, pharmacological treatments administered during the visit and referrals, often necessitated by resource limitations. Snakebite cases were identified using the International Classification of Diseases, Tenth Revision (ICD-10) code T63.0, as documented in the medical records.[5] The appropriateness of antivenom administration was also reviewed and extracted from these records.

As per the Queen Saovabha Memorial Institute (QSMI) guidelines, the criteria for administering hematotoxin antivenom are as follows: (1) a VCT exceeding 20 minutes; (2) a 20-minute WBCT without clot formation; (3) a platelet count below 50×10^9/L; (4) an INR over 1.2; (5) occurrence of systemic bleeding; and (6) the development of compartment syndrome requiring fasciotomy. The recommended dosage is between 3 and 5 vials for each administration, with the infusion lasting between 30 and 60 minutes.[16, 17] For neurotoxic antivenin, the indications include signs of muscle weakness, ptosis, and confirmed bites from the banded krait or Malayan krait. The recommended dosage is 5-10 vials per administration, with an infusion duration of 30-60 minutes. Indications for intubation incorporate a peak flow measurement below 200 L/min, dysphagia, respiratory muscle weakness, and ptosis characterized by a palpebral fissure less than 0.5 cm.[16] The seasonal classifications are summer (February to April), rainy season (May to October), and winter (November to January). The typical serum sodium range is 135-145 mmol/L, potassium is within 3.6-5.1 mmol/L, and bicarbonate is between 22 and 29 mmol/L. [18]

Statistical Analysis

Data were analyzed using StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC. The normality of the data was evaluated using the Kolmogorov-Smirnov test.[19] Baseline characteristics were investigated using descriptive statistics. Continuous data were presented as mean with standard deviation (SD) or median with interquartile range (IQR), while categorical data were expressed as frequency and percentage. The independent t-test was employed for continuous variables, and the Mann-Whitney U test was utilized for comparing continuous variables. Categorical variables were compared using Pearson's chi-squared test as appropriate. A two-sided p-value of less than 0.05 was considered to indicate statistical significance.

Ethics Considerations

The Institutional Review Board of the Royal Thai Army Medical Department conforms to international guidelines such as the Declaration of Helsinki, the Belmont Report, Council for International Organizations of Medical Sciences Guidelines, and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use-Good Clinical Practice (ICH-GCP), which reviewed and approved the study (Approval no. S029h/66_Exp). Given that the study utilized secondary data, the requirement for documenting informed consent was waived, and the Institutional Review Board of the Royal Thai Army Medical Department authorized this waiver.

Results

Baseline Characteristics of Participants

A total of 225 participants were included in the study. The median age of these participants was 39 (IQR 26-53 years) (**Table 1**). Of the participants, 145 (64.4%) were males. A rising trend in snakebite incidents was observed from 2014 to 2023, with a notable decrease from 2019 to 2021 (**Figure 1**). The proportion of bites from Russell's viper (56.5% of 23 cases) and cobra (50.0% of 24 cases) was higher between 2021 and 2023 compared to the period before 2020 (**Table 1**). **Figure 2** shows that 80.71% of the bites occurred during the rainy (44.4%) or summer (36.3%) seasons. Almost half of the bites (42.6%) occurred between 3.00 PM and 9.00 PM (**Figure 3**). Most patients (57.4%) reached the ED within 30 minutes of being bitten (**Figure 4**). Most patients presented with fang marks, with 55 patients having marks on their upper extremities (24.4%) and 154 on their lower extremities (68.4%). Notably, 10 out of 24 patients bitten by cobras experienced venom sprayed into their eyes (41.7%) but without systemic symptoms. Pain and swelling were common, with 56 (24.9%) patients experiencing pain and 36 (16.0%) reporting swelling (**Table 1**). Three patients reported ptosis, two experienced dyspnea, and two were diagnosed with impending compartment syndrome during their ED visit (**Table 1**).

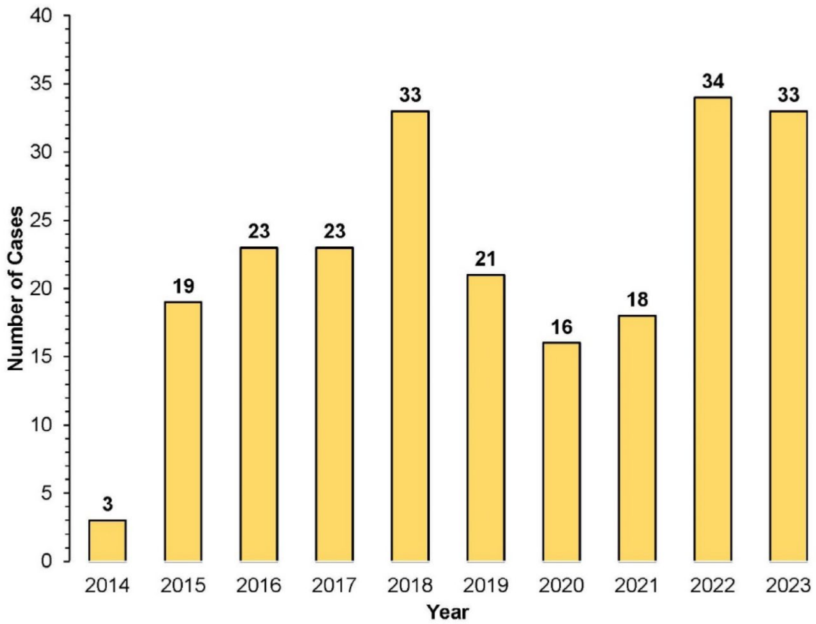

Figure 1. Trends in snakebite cases at Phattananikom Hospital, Lopburi, Thailand, from 2014 to 2023.

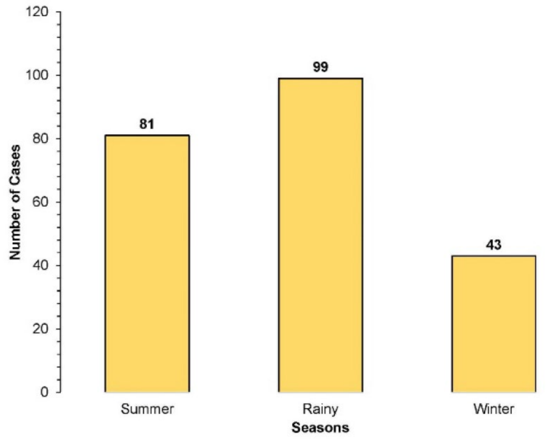

Figure 2. Seasonal distribution of snakebite cases at Phattananikom Hospital, Lopburi, Thailand. Summer: February to April, Rainy season: May to October, and Winter: November to January

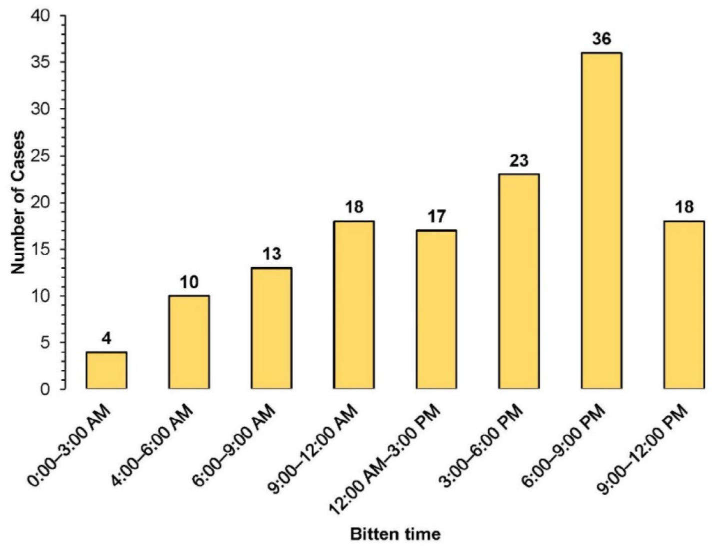

Figure 3. The bitten time of snakebite cases visiting Phattananikom Hospital in Central Thailand

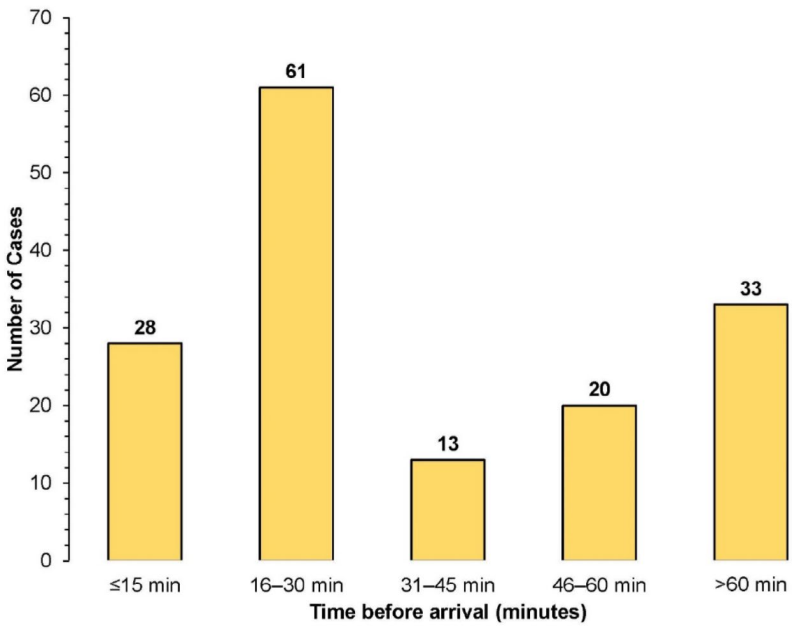

Figure 4. Time taken to reach the the emergency department, Phattananikom Hospital after snakebites.

Table 1. The characteristics of snakebite patients in Pattananikom Hospital, Lopburi, Thailand, stratified by snake type.

Characteristics	Total	Malayan pit viper	Russell's viper	Green pit viper	Cobra	Malayan krait	Other nonvenomous	Unknown
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total	225 (100.0%)	4 (100.0)	23 (100.0)	16 (100.0)	24 (100.0)	2 (100.0)	34 (100.0)	122 (100.0)
Year								
2014-2017	68 (30.5)	1 (25.0)	4 (17.4)	1 (6.7)	6 (25.0)	1 (50.0)	10 (29.4)	45 (37.2)
2018-2020	70 (31.4)	2 (50.0)	6 (26.1)	6 (40.0)	6 (25.0)	1 (50.0)	13 (38.2)	36 (29.8)
2021-2023	85 (38.1)	1 (25.0)	13 (56.5)	8 (53.3)	12 (50.0)	0 (0.0)	11 (32.4)	40 (33.1)
Sex								
Male	145 (64.4)	3 (75.0)	19 (82.6)	9 (56.3)	16 (66.7)	2 (100.0)	23 (67.7)	73 (59.8)
Female	80 (35.6)	1 (25.0)	4 (17.4)	7 (43.8)	8 (33.3)	0 (0.0)	11 (32.4)	49 (40.2)
Admission								
Outpatient	40 (17.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)	18 (52.9)	21 (17.2)
Admit	149 (66.2)	3 (75.0)	6 (26.1)	14 (87.5)	17 (70.8)	0 (0.0)	16 (47.1)	93 (76.2)
Refer	36 (16.0)	1 (25.0)	17 (73.9)	2 (12.5)	6 (25.0)	2 (100.0)	0 (0.0)	8 (6.6)
Bitten area								
Trunk	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Upper extremities	55 (24.4)	0 (0.0)	6 (26.1)	6 (37.5)	3 (12.5)	1 (50.0)	12 (35.3)	27 (22.1)
Lower extremities	154 (68.4)	4 (100.0)	17 (73.9)	10 (62.5)	11 (45.8)	1 (50.0)	20 (58.8)	91 (74.6)
Eye	10 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	10 (41.7)	0 (0.0)	0 (0.0)	0 (0.0)
Head	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Not seen	4 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (5.9)	2 (1.6)
Clinical manifestation								
Local pain	56 (24.9)	1 (25.0)	15 (65.2)	8 (50.0)	7 (29.2)	0 (0.0)	29 (85.3)	25 (20.5)
Swelling	36 (16.0)	1 (25.0)	18 (78.3)	6 (37.5)	23 (95.8)	2 (100.0)	4 (11.8)	13 (10.7)
Erythema	26 (11.6)	3 (75.0)	20 (87.0)	14 (87.5)	1 (4.2)	0 (0.0)	4 (11.8)	15 (12.3)
Compartment syndrome	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.6)
Dyspnea	2 (0.9)	0 (0.0)	1 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
Ptosis	3 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.3)	0 (0.0)	0 (0.0)	1 (0.8)

Table 1. The characteristics of snakebite patients in Pattananikom Hospital, Lopburi, Thailand, stratified by snake type. (Cont.)

Characteristics	Total	Malayan pit viper	Russell's viper	Green pit viper	Cobra	Malayan krait	Other non-venomous	Unknown
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Treatment								
Antibiotics	186 (82.7)	4 (100.0)	9 (39.1)	15 (93.8)	15 (62.5)	0 (0.0)	33 (97.1)	110 (90.2)
Pain control	187 (83.1)	4 (100.0)	9 (39.1)	14 (87.5)	17 (70.8)	0 (0.0)	33 (97.1)	110 (90.2)
Tetanus	72 (32.00)	2 (50.0)	4 (17.4)	3 (18.8)	0 (0.0)	0 (0.0)	18 (52.9)	45 (36.9)
Platelet (×10^9/L)								
Mean±SD	254.7±74.4	269.0±76.7	202.0±83.1	238.6±51.3	253.0±82.2	284.0±66.5	267.5±51.7	262.7±76.0
≥150x10^9/L	208 (93.7)	4 (100.0)	17 (73.9)	16 (100.0)	22 (95.7)	2 (100.0)	33 (100.0)	114 (94.2)
<150x10^9/L	14 (6.3)	0 (0.0)	6 (26.1)	0 (0.0)	1 (4.4)	0 (0.0)	0 (0.0)	7 (5.8)
Serum creatinine (mg/dL)								
Normal (<1.2)	173 (91.5)	2 (100.0)	19 (86.4)	14 (93.3)	20 (87.0)	2 (100.0)	24 (82.8)	92 (85.8)
Elevated (≥1.2)	16 (8.5)	0 (0.0)	3 (13.6)	1 (6.7)	3 (13.0)	0 (0.0)	5 (17.2)	4 (4.2)
Serum sodium (mmol/L)								
No hyponatremia (≥135)	180 (85.7)	3 (75.0)	18 (78.3)	14 (93.3)	20 (90.9)	2 (100.0)	28 (90.3)	95 (84.1)
Hyponatremia (<135)	30 (14.3)	1 (25.0)	5 (21.7)	1 (6.7)	2 (9.1)	0 (0.0)	3 (9.7)	18 (15.9)
Serum potassium (mmol/L)								
No hypokalemia (≥3.5)	149 (70.9)	1 (25.0)	8 (34.8)	13 (86.7)	16 (72.7)	2 (100.0)	26 (83.9)	83 (73.5)
Hypokalemia (<3.5)	61 (29.1)	3 (75.0)	15 (65.2)	2 (13.3)	6 (27.3)	0 (0.0)	5 (16.1)	30 (26.6)
Serum bicarbonate (mmol/L)								
No metabolic acidosis (≥22)	156 (74.3)	2 (50.0)	15 (65.2)	12 (80.0)	15 (68.2)	2 (100.0)	26 (83.9)	84 (74.3)
Metabolic acidosis (<22)	54 (25.7)	2 (50.0)	8 (34.8)	3 (20.0)	7 (31.8)	0 (0.0)	5 (16.1)	29 (25.7)

IQR: interquartile range; SD: standard deviation

Regarding the laboratory results from the patient's initial visit to the ED shown in **Table 1**, average platelet levels were significantly lower in patients bitten by Russell's viper compared to those bitten by other snake species (202.00 ±83.11×10^9/L for Russell's viper V.S.260.78± 71.08×10^9/L for other non-Russell's viper snakebites; p=0.001). Elevated serum creatinine levels were observed in 16 out of 225 patients (8.5%). However, the elevation was not statistically significantly associated with any specific snake species. Hyponatremia was present in 30 patients (14.3% of 225), with no significant difference between each snake species. Additionally, hypokalemia was detected in 61 patients (29.1% of 225), with a more significant proportion in those bitten by Russell's viper (65.2% of 23 patients; p=0.001).

Pharmacotherapy and Other Treatments for Snakebite Patients

Antibiotics were prescribed to 186 patients (82.7% of 225), with amoxicillin/clavulanic acid being the most used, and clindamycin administered to patients with penicillin allergies. For pain management, 187 patients (83.1% of 225) received a combination of paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioid derivatives (**Table 1**). Additionally, patients who had venom sprayed into their eyes by cobras were treated with copious saline irrigation, followed by chloramphenicol ointment. Regarding prehospital management, only one patient in 2015 reported using mouth suction after being bitten on the back of the hand. Other prehospital methods were not documented, such as tourniquet application and treatment by traditional healers.

Antivenom Treatment and Management

Out of 43 hematotoxic snakebites, 12 doses of hematotoxin antivenom were administered, including 10 doses of Russell's viper monovalent antivenom and two doses of green pit viper monovalent antivenom (**Table 2**). The indications for antivenom administration in cases of hematotoxic snake envenoming were as follows: an INR greater than 1.2 in 10 patients (23.3%), followed by systemic bleeding in 5 patients (11.6%), prolonged VCT in 2 patients (4.7%), and a platelet count below 50×109/L in one patient (2.3%). In cases of unidentified snakebites, seven patients (5.7%) had a prolonged INR, two patients (1.7%) had platelet counts below 50×109/L, two patients (1.6%) were diagnosed with impending compartment syndrome, and one patient (0.8%) exhibited prolonged VCT. Consequently, ten patients (8.3%) met the criteria for antivenom administration but did not receive it due to the unavailability of polyvalent antivenom (**Table 2**).

Table 2. Prevalence of hematotoxin antivenom indications among snakebite patients at Pattananikom Hospital, Lopburi, Thailand.

Characteristics	Hematotoxic snake n (%)	Unknown snake n (%)
Total	43 (100.0)	122 (100.0)
Indications		
Prolonged VCT	2 (4.7)	1 (0.8)
Unclotted 20 WBCT	*N/A	*N/A
Platelet < 50×10^9/L	1 (2.3)	2 (1.7)
INR>1.2	10 (23.3)	7 (5.7)
Systemic bleeding	5 (11.6)	0 (0.0)
Compartment syndrome	0 (0.0)	2 (1.6)
Antivenom administration	12 (27.9)	0 (0.0)
Antivenom type		
MPV monovalent AV	0 (0.0)	0 (0.0)
RV monovalent AV	10 (23.3)	0 (0.0)

Table 2. Prevalence of hematotoxin antivenom indications among snakebite patients at Pattananikom Hospital, Lopburi, Thailand. (Cont.)

Characteristics	Hematotoxic snake n (%)	Unknown snake n (%)
GPV monovalent AV	2 (4.7)	0 (0.0)
Appropriate administration		
Correct indication	10 (23.3)	0 (0.0)
Given with no indication	1 (2.3)	0 (0.0)
Have an indication but not given	2 (4.7)	10 (8.3)
Appropriate dosage	12 (27.9)	0 (0.0)

VCT: venous clotting time; WBCT: whole blood clotting time; INR: international ratio; AV: antivenom; MPV: Malayan pit viper; GPV: green pit viper; RV: Russell's viper;* the hospital does not test for unclotted 20 WBCT.

Among the 26 patients bitten by neurotoxic snakes, two (7.7%) exhibited ptosis, and one (3.9%) displayed muscle weakness. Another common indication was a bite from a Malayan krait (7.7%) (**Table 3**). Due to the unavailability of other types of antivenom, only one patient received cobra monovalent antivenom. Three patients (2.5%) bitten by unidentified snakes had indications for neurotoxin antivenom. However, they were referred elsewhere due to the unavailability of neuropolyvalent antivenom. Overall, 16 out of 29 patients (55.2%) with indications for antivenom did not receive it, with 15 cases attributed to the unavailability of polyvalent antivenom (**Table 4**).

Among the 13 participants who received antivenom (**Table 4**), 10 patients were treated with Russell's viper monovalent antivenom, totaling 40 vials (ranging from 3 to 5 per patient). Two patients received green pit viper antivenom using eight vials. One patient was administered 10 vials of cobra monovalent antivenom. Due to the severity of their conditions, all patients requiring more advanced medical attention did not receive a second dose of antivenom. Conversely, patients indicated for a second dose of antivenom were referred for further treatment.

Patient Characteristics Stratified by Referral Status in Snakebite Cases

Thirty-six cases were referred, with 55.6% of those referrals occurring between 2021 and 2023 ($p = 0.026$) (**Table 5**). The time before arrival and arrival time did not significantly differ between the referred and non-referred groups. Over half of the referred cases (55.6%) involved bites from hematotoxic snakes (p=0.001). Neurotoxic snakes bit eight patients (22.2%), and eight additional cases involved snakebites from unidentified species. Among the 14 cases with thrombocytopenia, eight cases with thrombocytopenia (57.1%) were referred (p=0.001), and all cases presenting with systemic bleeding (5 patients), dyspnea (2 patients), ptosis (3 patients), or diagnosed with compartment syndrome (2 patients) were also referred. Furthermore, a high proportion of hypokalemia was marked in referred cases (44.1%; p=0.034). The median serum creatinine levels were 0.94 (IQR: 0.80-1.08) for referred cases and 0.84 (IQR: 0.72-1.03) for non-referred cases (p=0.147).

Discussion

Snakebite envenoming is a globally neglected tropical disease leading to significant mortality and mobility due to severe clinical outcomes. Prompt prehospital management, including first aid, resuscitation, thorough physical and laboratory assessments, and timely administration of antivenom or other pharmacological treatments, can prevent fatalities and reduce disabilities.

Previous nationwide epidemiological surveys on snakebites in Thailand were performed from 1990 to 2010.[7, 20, 21] However, Thailand has

Table 3. Prevalence of neurotoxin antivenom indications among patients with snakebites at Pattananikom Hospital, Lopburi, Thailand.

Characteristics	Neurotoxin snake n (%)	Unknown snake n (%)
Total	26 (100.0)	122 (100.0)
Indication for intubation		
Dysphagia	0 (0.0)	1 (0.8)
Peak flow<200L/min	0 (0.0)	1 (0.8)
Respiratory muscle weakness	0 (0.0)	1 (0.8)
Ptosis	2 (7.7)	1 (0.8)
Indication for antivenom		
Muscle weakness	1 (3.9)	1 (0.8)
Ptosis	2 (7.7)	1 (0.8)
Bitten by branded krait	0 (0.0)	0 (0.0)
Bitten by Malayan krait	2 (7.7)	0 (0.0)
Antivenom administration	1 (3.9)	0 (0.0)
Antivenom type		
Cobra monovalent AV	1 (3.9)	0 (0.0)
Appropriate administration		
Correct indication	1 (3.9)	0 (0.0)
Given with no indication	0 (0.0)	0 (0.0)
Have an indication but not given	3 (11.5)	3 (2.5)
Appropriate dosage	1 (3.9)	0 (0.0)

AV: antivenom.

Table 4. Patients with antivenom indications and their management following snakebites at Pattananikom Hospital, Lopburi, Thailand.

Characteristics	n (%)
Total	29 (100.0)
Admission	
Outpatient	0 (0.0)
Admit	7 (24.1)
Refer	22 (75.9)
Appropriate administration	
Correct indication	12 (41.4)
Given with no indication	1 (3.5)
Have an indication but not given	16 (55.2)

Table 5. Referral of snakebite cases in Pattananikom Hospital in Central Thailand.

Variables	Non-refer	Refer	*p*-value*
	N (%)	N (%)	
Total	189 (100.0)	36 (100.0)	
Year			0.026
2014-2017	63 (33.7)	5 (13.9)	
2018-2020	59 (31.6)	11 (30.6)	
2021-2023	65 (34.8)	20 (55.6)	
Bitten season			0.322
Summer	65 (34.8)	16 (44.4)	
Rainy	83 (44.4)	16 (44.4)	
Winter	39 (20.9)	4 (11.1)	
Age (years)			
Median (IQR)	39 (25.0-53.0)	39 (28.5-54.0)	0.628
Sex			0.068
Male	117 (61.9)	28 (77.8)	
Female	72 (38.1)	8 (22.2)	
Time before arrival			0.194
60 minutes and below	101 (80.8)	21 (70.0)	
Over 60 minutes	24 (19.2)	9 (30.0)	
Arrival time			0.252
0:00 AM–7:59 AM	16 (8.5)	6 (16.7)	
8:00 AM–3:59 PM	81 (42.9)	12 (33.3)	
4:00 PM–11:59 PM	92 (48.7)	18 (50.0)	
Snake type			0.001
Unknown	114 (60.3)	8 (22.2)	
Neurotoxin	18 (9.5)	8 (22.2)	
Hematotoxin	23 (12.2)	20 (55.6)	
Other nonvenomous	34 (18.0)	0 (0.0)	
Thrombocytopenia (<150x10^9/L)			0.001
No	180 (96.8)	28 (77.8)	
Yes	6 (3.2)	8 (22.2)	
Clinical manifestation			
Systemic bleeding	0 (0.0)	5 (13.9)	0.001
Compartment syndrome	0 (0.0)	2 (5.6)	0.001
Dyspnea	0 (0.0)	2 (5.6)	0.001
Ptosis	0 (0.0)	3 (8.3)	0.001
Serum creatinine			
Median (IQR)	0.84 (0.7-1.0)	0.94 (0.8-1.1)	0.147
Serum sodium (mmol/L)			0.646
No hyponatremia (≥135)	150 (85.2)	30 (88.2)	
Hyponatremia (<135)	26 (14.8)	4 (11.8)	

Table 5. Referral of snakebite cases in Pattananikom Hospital in Central Thailand. (Cont.)

Variables	Non-refer	Refer	*p*-value*
	N (%)	N (%)	
Serum potassium (mmol/L)			0.034
No hypokalemia (≥3.5)	130 (73.9)	19 (55.9)	
Hypokalemia (<3.5)	46 (26.1)	15 (44.1)	
Serum bicarbonate (mmol/L)			0.333
No metabolic acidosis (≥22)	133 (75.6)	23 (67.7)	
Metabolic acidosis (<22)	43 (24.4)	11 (32.4)	

*The chi-square test is used to compare categorical data, and the Mann-Whitney U test is employed to compare medians.

undergone rapid urbanization, which may have altered the distribution of snakebites over time, making older reports less representative of current trends. In this study, a total of 225 medical files for snakebite patients visiting the ED at Pattananikom Hospital, a community hospital in Lopburi, were collected. Under the Ministry of Public Health (MoPH), Thailand's healthcare system includes 833 hospitals, 33 regional hospitals, 83 general hospitals, and 717 community hospitals, with the community hospitals accounting for 86% of the total hospitals. Pattananikom Hospital is a community hospital with approximately 60-90 beds that serves a vital role in snakebite management.[15] Of the 225 snakebite cases, 103 were identified as having been bitten by cobras and Russell's vipers, the two most common snake species. Indeed, green pit vipers were previously proven to be the most frequent snakebite cases in Central Thailand.[22] Interestingly, a 2005 study mentioned that cobras were comparatively less common in Lopburi and more prevalent in the southern and northern provinces of Nakhon Si Thammarat and Nakhon Sawan.[20] This discrepancy suggests that further investigation into shifts in snakebite distribution in Thailand is necessary.

The current study observed a growing trend in snakebite cases from 2014 to 2023, with a notable decline between 2019 and 2021 **(Figure 1).** This decrease may have been caused by the COVID-19 pandemic, which led to lockdowns, restricting movement, and encouraging people to stay indoors. Like previous studies, snakebites were most common during the rainy season, with fewer cases reported in the winter.[5,17]

Most patients were bitten in the evening between 3:00 PM and 9:00 PM, possibly due to increased outdoor activity. Almost 80% of the patients reached the ED within 60 minutes of being bitten by a snake (**Figure 4**), with a median time of 29 minutes. In contrast, a previous study in Bangkok reported a longer median arrival time of 55 minutes, possibly due to heavier traffic than in Lopburi.[22] The time to ED arrival in our study was longer than that in Wongthongkam et al.'s study.[21] This may be explained by the fact that most snakebite data was gathered in isolated rural areas.

Among the 26 patients bitten by neurotoxic snakes, two (7.65%) presented with ptosis, and one (3.85%) showed muscle weakness. Neurotoxic snakes release neurotoxins that rapidly bind to nicotinic receptors, causing symptoms such as muscle weakness, ptosis, dysphagia, and potentially fatal respiratory failure.[6] Some snake venoms exert cytotoxic effects in addition to hepatotoxic and neurotoxic effects, leading to tissue necrosis and compartment syndrome.[9]

Interestingly, 10 of the 24 patients bitten by cobras experienced venoms spraying into their eyes. Venom spraying, or "venom spitting," is an uncommon but well-documented defensive reflex used by cobras to eject venom onto approaching threats.[23] The cobras can project venom onto targets up to 1.5 to 3 meters away.[24, 25] In Thailand, the spitting cobra species include *Naja kaouthia* (the monocled cobra), *Naja siamensis* (the Indochinese spitting cobra), *Naja sumatrana* (the Equatorial or golden spitting cobra), and *Naja fuxi*, a species newly identified in Thailand.[26] The spitting cobras in Thailand are mostly *Naja siamensis* and *Naja sumatrana*.[26] Though immediate irrigation with water generally prevents severe symptoms, some patients may still experience eye burns or corneal injuries.[27] Therefore, developing prehospital and emergency management guidelines for citizens and health personnel would benefit.

While this study reported prompt irrigation and topical antibiotics for venom-spitting injuries, the WHO recommends copious irrigation and standardized care protocols, underscoring the need for improved prehospital and emergency management guidelines.[28] Previous studies reported no significant difference in treating ophthalmic injuries caused by spitting cobra venom between topical dexamethasone, antivenom, and untreated control eyes.[28, 29] Prophylactic antibiotic drops can reduce the risk of multiple corneal erosions progressing to full corneal ulcers or keratitis, which may lead to perforation or secondary bacterial infection.[30] Topical anesthetics and mydriatic drops can be used to manage pain. The former is particularly useful for overcoming blepharospasms and facilitating effective eye irrigation.[28] In this study, all patients who experienced venom spitting received saline irrigation within an hour of arrival, followed by topical antibiotics. There were no reports of acute ocular complications or referrals.

Envenomation by vipers typically excites hematotoxicity, inducing bleeding and significant clinical outcomes.[31] Russell's vipers, green pit vipers, and Malayan pit vipers are known for causing thrombocytopenia, increased vascular fragility, dysfunctional platelets, coagulopathy, and enhanced fibrinolysis.[17, 22, 32] Their venoms can also lead to snake venom-induced consumption coagulopathy.[8] Consequently, patients bitten by hematotoxic snakes in this study exhibited a more significant proportion of prolonged INR, thrombocytopenia, and systemic bleeding. These factors were also strongly associated with increased referrals. Additionally, consistent with previous studies, hypokalemia was detected in more severe cases of snakebites, particularly those involving both neurotoxic and hematotoxic venoms.[33–35] This may result from potassium shifting into cells due to beta-adrenergic stimulation, a consequence of autonomic dysfunction.[33, 36] Bleeding tendency and coagulopathy are predictors of mortality in patients with poisonous snakebites. Therefore, referring high-risk cases to higher-level hospitals for specialized management is crucial.[14] Moreover, future studies should consider hypokalemia as a potential predictor of severe outcomes in snakebites. Elevated serum creatinine levels were observed following envenomation by Russell's viper (13.6%), green pit viper (6.7%), and cobra (13.0%), potentially indicating acute kidney injury based on initial laboratory findings. However, additional renal function tests at later stages may be necessary to assess better and prevent nephrotoxicity associated with snakebite envenomation.[37]

Pattananikom Hospital only had monovalent antivenoms for cobras, green pit vipers, and Russell's vipers available. Consequently, a significant reason for referrals in this study was the absence of polyvalent antivenom for unidentified snakebites. Conversely, in Southern Thailand, where the Malayan pit viper is most common, specific antivenoms can be administered for patients with hematologic symptoms from unidentified snakes.[17] Urban hospitals in Thailand reported a relatively higher proportion of adequate and correctly administered antivenom than the present study.[5, 12, 38] This is attributed to robust antivenom supply chains supported by efficient production, distribution systems, and regulatory oversight. In contrast, rural areas face limited access to specific monovalent and polyvalent antivenoms, highlighting a critical disparity.[39]

In this study, thirteen patients bitten by unidentified snakes with indications for antivenom were referred, potentially causing delays in antivenom administration. Prior studies have highlighted the benefits of early antivenom administration and revealed that delays could prompt higher mortality rates in hematotoxic and neurotoxic snakes.[40] Antivenom should ideally be administered within 6 hours of the snakebite to maximize its effectiveness.[41]

A study by Patikorn et al.[4] found that 69% of snakebite victims who require antivenom treatment in ASEAN countries receive it. Thailand has the lowest rate at less than 1% of untreated cases. However, this study remarked that a more significant proportion of snakebite victims at Pattananikom Hospital did not receive antivenom, likely due to the lack of polyvalent antivenom and limited availability of antivenom after referrals. Delays in antivenom administration significantly increase morbidity and mortality. Hence, it is essential to develop strategies to enhance the availability of antivenoms, particularly polyvalent antivenom, in hospitals that frequently encounter unidentified toxic snakes; this would improve outcomes and reduce overall production costs.[10] Moreover, the WHO highlights the role of supportive care, including pain management, respiratory support for neurotoxic envenoming, and thorough wound care for cytotoxic injuries. This study partially addressed these, but the lack of mechanical ventilators and comprehensive wound care in community hospitals indicates that further alignment with WHO recommendations is needed.[42]

Several strategies can reduce delays and improve snakebite outcomes by addressing antivenom availability challenges in community hospitals. Establishing regional stockpiles of essential monovalent and polyvalent antivenom and utilizing mobile health technologies may assist in timely access in remote areas.[43] Training healthcare providers on early snakebite recognition and rapid treatment protocols and investing in diagnostic tools for envenomation and snake identification can further minimize delays.[44] Community education on first aid and prompt medical care enhances hospital presentation times.[45] Additionally, collaboration with organizations like the WHO to improve antivenom production and distribution is vital. These measures collectively strengthen community hospitals' capacity to manage snakebites and reduce associated morbidity and mortality.

Similar to earlier studies in Southern Thailand, most patients received prophylactic antibiotics such as amoxicillin/clavulanic acid and dicloxacillin.[5] While the routine use of antibiotics in snakebite cases remains controversial, Thailand's clinical practice guidelines recommend amoxicillin/clavulanic acid only when signs of infection are present.[16] However, previous studies demonstrated that amoxicillin-clavulanate may be ineffective in preventing secondary infections after snakebite due to common bacterial resistance at snakebite sites and snake oral microbiota. Contrarily, third-generation cephalosporins are typically more effective.[46,47] However, the choice of antibiotics ultimately depends on the clinician's discretion. Prophylactic antibiotics are likely justified, given the risks of secondary infections, especially in rural areas.[48] Further research on identifying bacterial species in snakebite wounds in Thailand and their antibacterial resistance would help inform antibiotic choices in clinical management.

This study encountered some limitations that should be considered. Firstly, its cross-sectional design limited the ability to evaluate longitudinal changes and long-term outcomes after discharge. Future studies could adopt longitudinal data collection to assess snakebite outcomes more effectively. For example, this study's single time point collection of clinical laboratory data could have limited the detection of complications, such as acute kidney injury or long-term kidney function decline. Measuring serum creatinine multiple times, including 24 and 48 hours and during follow-up visits, could improve detection and monitoring. Secondly, the retrospective nature and the 10-year duration of the study may have led to missing data due to incomplete medical records. Thirdly, the reliance on the primary physician's report at the ED for arrival times, clinical manifestations, and diagnoses could introduce bias. Moreover, because the study relied on the initial medical review at the ED, information such as treatments administered during admission and home medications was not available. Fourthly, the study was conducted in a single hospital, limiting its generalizability to other regions.

Furthermore, the retrospective design and referral bias could have impacted the study's mortality estimation and the completeness of antivenom data, as severe cases are often referred to larger hospitals, potentially underestimating the mortality rate. Therefore, caution is needed when interpreting and applying the findings more broadly. Despite these limitations, this study provides valuable insights into the updated epidemiology and clinical management of snakebites in Lopburi Province, Central Thailand.

Conclusion

This study revealed the association between clinical profile and management of snakebites in a community hospital in Thailand, based on data from 225 snakebite patients collected over almost ten years. Urbanization might have altered the distribution of snake species compared to earlier studies, highlighting the need for a nationwide survey to assess these changes. Furthermore, awareness of the signs and symptoms of cobra envenoming and necessary intervention are required, particularly on venom ophthalmia. While monovalent antivenoms for medically crucial venomous snake species in the locality are readily available, the shortage of other monovalent and polyvalent antivenom can cause delays in treatment, potentially leading to higher mortality. Consequently, developing strategies to improve the availability and distribution of antivenoms is crucial for optimal management of snakebite envenoming.

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Availability of Data and Materials

The datasets used and/or analyzed during the current are available from the authors upon reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

PS, TC, OK, SL, KJ, WC, and JC conceptualized the study. PS, TC, and OK collected the data. SL analyzed the data, and SL and PS wrote the first draft. All authors contributed to and approved the final version.

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