Systematic Review

HEMOCOAGULATION CONDITIONS ASSOCIATED WITH VENOM-INDUCED CONSUMPTION COAGULOPATHY DUE TO SNAKEBITE IN HUMANS

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ABSTRACT

Snakebite remains an underreported health hazard worldwide. The most common effect of snakebite envenomation globally are hematological disorders, with venom-induced consumption coagulopathy (VICC) being the most prevalent and significant condition. This review aims to explore the hematological aspects of snakebite, with a focus on venom-induced consumption coagulopathy. This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines by searching multiple databases, namely PubMed, ScienceDirect, and Google Scholar. The inclusion criteria for this review were studies on snakebite envenomation in humans with a discussion of relevant cases. Additionally, the included studies were conducted between 2010 and 2023 and written in English. Studies on animal models were excluded. The search terms used were "venom-induced consumption coagulopathy AND snake". The critical appraisal was performed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports and the Mixed Methods Appraisal Tool (MMAT). The findings were presented as a qualitative synthesis of 14 articles covering 316 patients and various types of snakebite. The studies on snakebite came from different countries, but mostly from Sri Lanka. The snake species varied, with certain species found only in certain areas. The subjects fell into different age groups, from children to the elderly. The majority of the subjects were male. The youngest subject was six years old, while the oldest was 70 years old. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were the most discussed variables. Some of the studies demonstrated an increase in PT and APTT, although other studies reported contrasting findings. In conclusion, different types of snakebite have different effects on hemocoagulation status.

Keywords: Hematology; abnormalities; snakebite; mortality; venom-induced consumption coagulopathy

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Highlights:
1. This review comprehensively highlighted aspects of hematologic abnormalities in snakebites, a topic that remains understudied globally.
2. This review contributes insights into the field of snakebite research and improves the management of snakebites by examining the diverse effects of different types of snakebites on hemocoagulation status.

INTRODUCTION

Snakebite continues to be a globally underestimated hazard. According to the World Health Organization (2016), there are around 5.4 million snakebites annually, of which 2.7 million are venomous. These venomous snakebites have a mortality rate of 5%, resulting in 137,880 deaths per year. Among 63,454 Nepali people living in 13,879 households throughout 249 villages, there were 166 reported cases of snakebites during the course of 12 months. Out of the recorded snakebite cases, 48.8% resulted in poisoning, while 7.8% ended in fatalities. These are the first epidemiological estimates of snake bite venom in both humans and domestic animals in the Terai lowlands of Nepal. The findings call for strengthening preventive measures and better access to life-saving care (Alcoba et al. 2022).

According to Noutsos et al. (2020), hematologic disorders are the most common effects of snakebite poisoning globally. Among the hematologic disorders, venom-induced consumption coagulopathy (VICC) is the most prevalent and significant condition. Other hematologic disorders include anticoagulant coagulopathy and thrombotic microangiopathy. VICC is the activation of the coagulation pathway induced by a procoagulant toxin. Hematologic disorders refer to abnormalities in the blood, including problems with red blood cells, white blood cells, platelets, bone marrow, lymph nodes, and the spleen (Berling & Isbister 2015, Russell et al. 2021).

Bleeding, especially fatal cerebral bleeding, is the main side effect of VICC. The role of antivenom in VICC is debatable and may only help envenomation caused by certain snake species. There is insufficient data available regarding the hemostasis dynamics in individuals suffering from VICC resulting from snake envenomation (Isbiter et al. 2010, Berling & Isbister 2015). In addition, some species may produce different clinical manifestations. Snakes are broadly classified into four groups: Hydrophidae, Elapidae, Viperidae, and Crotalidae (Setiabudy 2009). Snake venoms that cause coagulopathy can be classified as procoagulant venoms, anticoagulant venoms, platelet activity venoms, and vascular wall interactive venoms. The manifestations of coagulopathy may include the prolongation of plasma prothrombin time (PPT) and activated partial thromboplastin time (APTT), increased international normalized ratio (INR), hypofibrinogenemia, thrombocytopenia, and increased fibrin degradation products (McCleary & Kini 2013). Laboratory examination has an important role in monitoring patients to avoid complications. Furthermore, it is crucial to comprehend the manifestations of coagulopathy caused by diverse species in various regions. In light of this background, the aim of this review was to explore different aspects of hematologic abnormalities in snakebites, with a particular focus on VICC.

MATERIALS AND METHODS

This systematic review has been recorded in the International Prospective Register of Systematic Reviews (PROSPERO), with the registration number CRD42024551873. The conduct of this study followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Page et al. 2021). The data were collected in April 2024. We searched for articles in three databases: Google Scholar, ScienceDirect, and PubMed. The keywords used were “snakebite AND venom consumption-induced coagulopathy." We also searched using the synonyms of the words, such as "retention."

The study selection in this review was carried out with specific inclusion criteria, i.e., studies conducted in 2010–2023, published in English, and focused on the topic of snakebites in humans, with a discussion of relevant cases (Figure 1). The exclusion criteria for this study were animal studies, letters to editors, study reviews, preprints, and abstracts without full text. During the process of data collection, the authors independently performed title and/or abstract screening of the selected articles by utilizing standard forms in Microsoft Excel for Windows, version 2021 (Microsoft Inc., Redmont, WA, USA). The data obtained were combined into one folder, and then an assessment was performed. After each author analyzed all available articles, the analysis results were compared with one another (Tawfik et al. 2019).

The authors conducted a risk-of-bias assessment using critical appraisal tools. The research quality of case reports was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports. The quality of cross-sectional, experimental, prospective, and retrospective studies was analyzed using the Mixed Methods Appraisal Tool (MMAT) version 2018. The MMAT was specifically designed for reviews that include qualitative, quantitative, and mixed-methods studies (Hong 2018). The process of data abstraction and synthesis included several steps, beginning with the extraction of relevant results. These results were then sorted and carefully examined to identify sub-themes and themes. The synthesis method used was qualitative synthesis. The data arranged in Table 3 contain the characteristics of the selected studies, including the (1) author and year, (2) country, (3) research method, (4) snake type, (5) number of samples, (6) age, (7) sex category, and (8) finding.

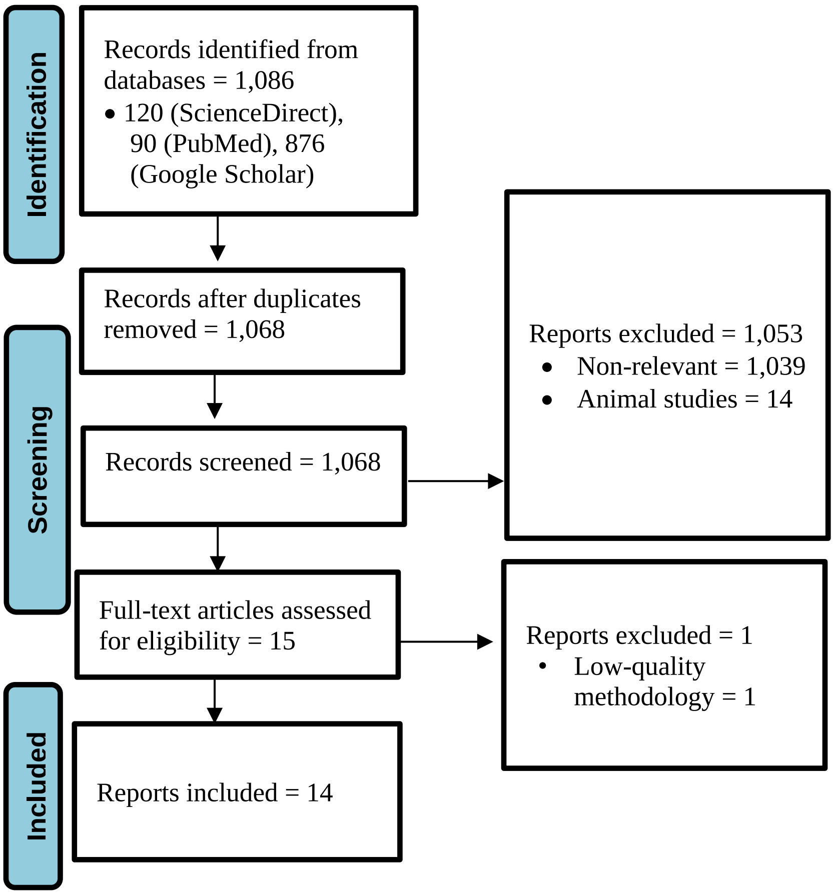

Figure 1. PRISMA flow diagram for the study selection.

RESULTS

After reviewing the titles and abstracts, we conducted a thorough examination of the full texts. Subsequently, a total of 14 articles were included in this systematic review. The PRISMA flow diagram shown in Figure 1 provides a visual representation of the study selection process and the reasons for exclusion. All of the included articles underwent quality assessment using critical appraisal tools, as shown in Tables 1 and 2. The summarized critical appraisal results showed that the quality of the studies was generally moderate to good.

The selected studies on snakebites were conducted in various countries, including India, Japan, Australia, South Korea, Sri Lanka, the Czech Republic, the USA, Vietnam, Taiwan, and Brazil. However, most of the studies were from Sri Lanka Priyankara et al. (2022).

The assessment also revealed variations in the types of snakes among the included studies. The studies reported that there were certain species that exclusively inhabit particular areas. In some of the selected studies, the researchers did not provide details regarding the types of snakes that were investigated.

The studies included in this systematic review mostly focused on subjects across a wide age range, spanning from pediatric to geriatric populations. The youngest subject in the studies was 6 years old, whereas the oldest was 70 years old. The largest proportion of the subjects were male.

The selected studies showed that certain types of snakebite had varying impacts on hemocoagulation status. The studies examined the hemocoagulation parameters of snakebites, particularly PT and APTT. Some of the studies revealed prolonged PT and APTT, while other studies documented different findings from the laboratory tests. Several studies reported an increase in the results of the PT/INR test, while other studies indicated that the examined parameters remained stable.

Table 1. Quality of the quantitative non-randomized studies.

Author, year	Assessment criteria					Total score
	Are the participants representative of the target population?	Are measurements appropriate regarding both the outcome and intervention (or exposure)?	Are there complete outcome data?	Are the confounders accounted for in the design and analysis?	During the study period, is the intervention administered (or exposure occurred) as intended?	
Johnston et al. (2013)	Yes	Yes	Yes	Yes	No	4
Moon et al. (2021)	Yes	Yes	Yes	Yes	No	4
Maduwage et al. (2013)	Yes	Yes	Yes	Yes	No	4
Valenta et al. (2022)	Yes	Yes	Yes	Yes	No	4
Silva et al. (2022)	Yes	Yes	Yes	Yes	No	4
Rathnayaka et al. (2020)	Yes	Yes	Yes	Yes	No	4
Dang et al. (2021)	Yes	Yes	Yes	Yes	No	4
Seifert et al. (2011)	Yes	Yes	Yes	Yes	No	4

Furthermore, the studies reported the presence of fibrinogen degeneration products (FDP) and observed a decrease in fibrinogen levels in snakebite victims. However, certain studies observed that platelet levels remained constant within the normal range, but other investigations identified cases of anemia among the patients. While some of the studies found that D-dimer concentrations were within the normal range, other studies observed that the D-dimer concentrations peaked at a median time of 63.5 hours. The studies showed that the 20-minute whole blood clotting test (WBCT20) failed to detect snakebite envenomation from certain types of snakes. Table 3 presents the characteristics of the assessed studies.

Table 2. Critical appraisal for the case reports.

Author, year	Were patient's demographic characteristics clearly described?	Was the patient's history clearly described and presented as a timeline?	Was the current clinical condition of the patient on presentation clearly described?	Were diagnostic tests or assessment methods and the results clearly described?	Was the intervention(s) or treatment procedure(s) clearly described?	Was the post-intervention clinical condition clearly described?	Were adverse events (harms) or unanticipated events identified and described?	Does the case report provide takeaway lessons?
Gopalakrishnan et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Ichiki et al. (2019)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Priyankara et al. (2022)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Wilson et al. (2024)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Chien et al. (2017)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
de Medeiros et al. (2021)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

DISCUSSION

According to the evaluated studies, distinct impacts on hemocoagulation status arose from snakebites from various types of snakes. The majority of the studies indicated an extension of PT and APTT, although some other studies reported differing findings from the laboratory examinations. In some species examined in the studies, different clinical manifestations were present. The classifications of snakes can be divided into four groups, i.e., Hydrophidae, Elapidae, Viperidae, and Crotalidae (Setiabudy 2009). Snake venoms that induce coagulopathy can be categorized into procoagulant venoms, anticoagulant venoms, platelet activity venoms, and vascular wall interactive venoms. The signs of coagulopathy may consist of the prolongation of PPT and APTT, elevation of INR, hypofibrinogenemia, thrombocytopenia, and a rise in fibrin degradation products. Complete blood tests, peripheral blood smears, and assessments of blood coagulation functions such as PT, APTT, fibrinogen, D-dimer, and INR levels can be conducted to determine the presence or absence of bleeding manifestations in snakebites (McCleary & Kini 2013, Puspaningtyas et al. 2022). Snakebites can lead to VICC, which refers to any coagulopathy resulting from the consumption of clotting factors by procoagulant toxins present in snake venom. The condition is attributed to the venom produced by various snake species, particularly the members of the *Viperidae*, *Elapidae*, and some *Colubridae* families. On the other hand, disseminated intravascular coagulation (DIC) occurs when the clotting pathway is activated and is associated with a very high mortality rate. VICC is characterized by a different pathogenic process involving specific enzyme activation. It requires a different treatment approach compared to DIC. However, VICC generally has a more benign course than DIC (Jeon et al. 2019).

Multiple studies in this systematic review observed an elevation in the PT/INR test results, although some other studies determined consistent test results. This was similar to the examination of fibrinogen degeneration products. Snakebite typically results in a decrease in fibrinogen levels. Fibrinogen, a glycoprotein produced by the liver, plays a role in the coagulation cascade (White 2023). Hemorrhage frequently arises as a complication in snakebite cases, primarily as a result of the venom released by most snake species. Complications occur through various coagulation pathways, which are indicated by PT and APTT associated with decreased fibrinogen levels due to consumptive coagulopathy. Bleeding resulting from snake venom can be caused by consumption coagulopathy and defibrinogenation, leading to reduced levels of fibrinogen, typically below 150 mg/dL (Greene 2021, Larréché et al. 2021). Fibrinogen will be converted by thrombin into fibrin, and as a balance process, fibrinolysis will occur in the body. Fibrinolysis is the process of plasmin hydrolytic enzyme activity that progressively breaks down fibrin and fibrinogen to reduce clots (thrombus). Plasmin, the main fibrinolytic enzyme that breaks down fibrinogen and fibrin, produces degeneration products in the form of fibronogen or fibrin degradation products, specifically fragments X, Y, D, E, and D-dimer. Normal individuals typically have plasma D-dimer levels below 200 mg/L. However, the presence of procoagulant venoms that activate the clotting pathway can significantly increase these levels. Australian elapid snake venom causes an increase in D-dimer levels 100 to 1,000 times higher than the upper normal limit. Russell's snake venom induces an increase in D-dimer levels, ranging from 10 to 100 times the upper normal limit. Snake venom that induces thrombin-like enzyme (TLE) activity results in fibrinogen consumption without the production of cross-linked fibrin, leading to an insignificant increase in D-dimer levels (Keohane et al. 2015, Berling & Isbister 2015).

The assessed studies showed that the platelet levels predominantly remained within the normal range. However, there were studies that reported the prevalence of anemia among the patients. A coagulopathic condition associated with microangiopathy hemolytic anemia (MAHA) causes an anemic state characterized by a decreased hemoglobin (Hb) level and increased reticulocytes on a complete blood examination (Orak et al. 2012). Thrombocytopenia and red blood cell fragmentation in peripheral blood smears can be markers of microangiopathic thrombosis. Peripheral blood smears can reveal the amount of spherocytes, anisocytosis, poikilocytosis, and rarely schistocytes. Spherocytes are small, round, thick, dense red blood cells that appear to have a slightly darker color and no clear zone or central pallor in the middle compared to normal red blood cells. The changes in red blood cells indicate toxin-induced spherocytic hemolytic anemia. This is different from microangiopathic hemolytic anemia, which occurs in disseminated intravascular coagulation and is characterized by erythrocyte fragmentation caused by damage to the erythrocyte due to partially blocked small blood vessels (Keohane et al. 2015).

In this systematic review, the selected studies were conducted in various countries, including India, Japan, Australia, South Korea, Sri Lanka, the Czech Republic, the USA, Vietnam, Taiwan, and Brazil. Snakebite cases in developing countries, such as Indonesia, often occur in rural areas with limited health facilities. This poses a challenge to performing complex laboratory tests, such as those used to examine the clotting time. The South-East Asia Regional Office (SEARO) of the World Health Organization (WHO) recommends conducting the 20WBCT for suspected cases of viper bites in facilities with limited resources. The test can be performed at the bedside by dripping 2 mL of venous blood onto a clean, detergent-free glass surface and leaving it for 20 minutes. The test result is considered positive for VICC if the blood coagulates within the specified time (World Health Organization 2016).

Table 3. Hemocoagulation condition in humans due to snakebite.

No	Author, year	Country	Research method	Type of snake	Number of samples	Age (y.o.)	Sex	Finding
1.	Gopalakrishnan et al. (2021)	India	Case report	*Echis carinatus sochureki*	1 patient	60	Male	In the coagulation profile analysis, prolonged PT and APTT were observed (>120 seconds, which is the detection limit) and persisted for seven days following snakebites. The local bleeding stopped within a day. The renal function and platelet levels remained normal.
2.	Ichiki et al. (2019)	Japan	Case report	*Rhabdophis tigrinus* (*yamakagashi* in Japanese)	1 patient	10	Male	At 30 minutes after poisoning, only the TAT complex level increased. At 90 minutes after poisoning, the APTT was prolonged, while the PT/INR and FDP increased. At 5.5 hours after poisoning, the APTT and PT/INR increased beyond the measurable range, while the fibrinogen levels fell below the detection limit.
3.	Johnston et al. (2013)	Australia	Prospective cohort study	Mulga snake (*Pseudechis australis*)	17 patients	Median: 37 (IQR: 6–70)	Male: 16 Female: 1	Anticoagulant coagulopathy was present in ten patients, as indicated by the abnormal APTT. The INR was normal in six patients and above the normal range in four patients. Eight patients had normal results for the fibrinogen and D-dimer tests. No patient had clinically significant bleeding. Acute hemolysis occurred in six patients. The median hemoglobin concentration decreased in six patients. Two patients had mild anemia, whereas three patients exhibited more severe anemia. No patient received red blood cell transfusions.
4.	Moon et al. (2021)	South Korea	Retrospective, observational study	The authors could not verify the causative snakes because of the retrospective design.	119 patients	≥18 (mean: 61)	Male: 66	Within three hours, 34 out of 119 patients developed VICC. In the VICC group, two patients required blood transfusions. Five patients with complete VICC presented with undetectable fibrinogen concentrations. Within 24 hours, three patients with complete VICC exhibited unmeasurable INR and APTT. In the VICC group, the median time for the most extreme readings was 10 hours for INR, 12 hours for APTT, and 16 hours for fibrinogen. D-dimer concentrations peaked at a median of 63.5 hours. The activities of factors II and X were significantly reduced, while factor V remained constant.

5.	Maduwage et al. (2013)	Sri Lanka	Retrospective cohort study	Sri Lankan hump-nosed pit viper (*Hypnale hypnale*)	80 patients	37 (IQR: 26–51)	Male: 48 Female: 32	The WBCT20 result was positive in one patient. There was an increase in the INR and APTT. The levels of fibrinogen, factor VIII, and factor V were low. D-dimer concentrations were slightly elevated. Factors II, VII, and X, as well as the vWF antigen, were normal. The snakebites in the study typically cause a mild coagulopathy that is often not detected by WBCT20.
6.	Priyankara et al. (2022)	Sri Lanka	Case report	Juvenile Russell's viper (*Daboia russelii*)	1 patient	70	Male	The WBCT20 result remained negative. However, the INR increased slightly to 1.6, and the APTT took 48 seconds. The highest INR was 1.8, recorded 41 hours after the bite, although it returned to the normal range on day 3. All the WBCT20 results were consistently negative, except for one positive case that occurred 39 hours post-bite.
7.	Valenta et al. (2022)	Czech Republic	Pilot study	Non-European *Viperidae* snakes: Great Lakes bush viper (*Atheris nitschei*), Malayan pit viper (*Calloselasma rhodostoma*), Eastern diamondback rattlesnake (*Crotalus adamanteus*) (two cases), Palestine saw-scaled viper (*Echis coloratus*), and Cyclades blunt-nosed viper (*Macrovipera schweizeri*)	6 patients	NA	NA	Following the envenomation caused by *Crotalus* and *Echis* vipers, the clotting durations for PT (INR), APTT, and TT were the most affected (>10, >180seconds, and >180 seconds, respectively). The clotting times were correlated with both the dramatic declines in FBG levels and the results of western blot analysis. Envenomations caused by *Atheris*, *Calloselasma*, and *Macrovipera* snakes did not result in any discernible extension of clotting times, despite the decrease in FBG levels. All instances exhibited a rise in D-dimer concentrations, with the highest concentrations observed following *Atheris* and *Echis* snakebites. A reduction in platelet counts was observed only in *Macrovipera* and *Calloselasma* envenomations. There was no discernible decrease in AT III activity.
8.	Wilson et al. (2024)	USA	Case report	*Protobothrops mangshanensis*	1 patient	46	Male	At approximately 6 hours post-envenomation (2 hours after the initiation of antivenom), the D-dimer concentration increased to 8.9 mg/L. Additionally, the fibrinogen was undetectable (<50 mg/dL), and the INR increased to 2.97.
9.	Silva et al. (2022)	Sri Lanka	Non-randomized observational study	Russell's viper (*Daboia russelii*)	39 patients (antivenom group), 5 patients (no	Antivenom: median 40 No	Male: 37	In the antivenom group, 27 (69%) out of 39 patients had an INR of <1.5 at 48 hours post-bite. In contrast, none (0%) of the five patients in the group that did not receive antivenom had an INR

					antivenom group)	antivenom: 34		below 1.5. The antivenom group had a more severe VICC, with the highest median INR of 13 and the lowest median fibrinogen concentration of 0.3 g/L. In comparison, the group that did not receive antivenom had the highest median INR of 2.2 and the lowest median fibrinogen concentration of 1.3 g/L.
10.	Rathnayaka et al. (2020)	Sri Lanka	Prospective study	Proven cases: Snake specimen identified Probable cases: Snake specimen not available	30 patients (n=500; 6%) Developed VICC: 17 (3%) confirmed cases and 13 (2%) probable cases	54.5 (confirmed case), 43.2 (probable case)	Confirmed cases Male: 11 (65%) Female: 6 (35%) Probable cases Male: 7 Female: 6	Out of the confirmed and probable cases, 28 (6%) had either delayed APTT and PT or elevated INR, while 27 (5%) exhibited both parameters. Among the confirmed cases, 10 patients (59%) had a PT that was initially unrecordable (>60/12 seconds), and 10 patients (59%) had an APTT of >60/25 seconds. *Hypnale nepa* snakebites did not increase WBCT20 results, PT, INR, or APTT. One patient (3%) experienced elevated coagulation resulting from *Hypnale zara* snakebite. Additionally, 14 patients (5%) exhibited high PT, INR, and APTT, and 15 patients (5%) tested positive during the WBCT20 following *Hypnale hypnale* snakebites.
11.	Dang et al. (2021)	Vietnam	Prospective study	*Trimeresurus cornutus*, *Deinagkistrodon acutus*, *Trimeresurus mucrosquamatus*, *Trimeresurus albolabris*, and undefined snake species	41 patients	41.27±14.72	Male: 61% Male-to-female ratio: 1.56:1	Platelet counts decreased in 14 (34.2%) of the 41 patients. Prothrombin levels declined in 16 cases (39%). APTT was prolonged in 7 cases (17.1%). INR increased in 12 cases (29.3%). Fibrinogen concentration decreased in 61% of the cases. In addition, 18 cases (43.9%) exhibited a severe fibrinogen decrease. Increased D-dimer concentrations were found in 36 cases (87.8%). The prevalence of DIC was the highest in *Trimeresurus albolabris* snakebite cases.
12.	Chien et al. (2017)	Taiwan	Case report	Green habu (*Viridovipera stejnegeri*)	1 patient	47	Male	On arrival at the emergency department, the patients exhibited a PT of >100 seconds (INR of >10), a PTT of >100 seconds, a fibrinogen level of <50 mg/dL, and a FDP level of >80 µg/mL. The laboratory examination revealed a platelet count of 142,000/µL.
13.	de Medeiros et al. (2021)	Brazil	Case report	Venomous snakes: *Bothrops jararaca* (*Serpentes*, *Viperidae*) Nonvenomous snakes: *Philodryas olfersii* (*Serpentes*, *Dipsadidae*)	2 patients	55 and 35	Male: 2	The laboratory tests showed that the *Philodryas olfersii* snakebite caused leukocytosis and an increase in D-dimer levels. However, there was normal coagulation, indicating a recently resolved coagulopathy. The *Bothrops jararaca* snakebite resulted in mild coagulopathy,

								leukocytosis, and increased D-dimer levels. In both cases, the WBCT20 results were normal. The *Philodryas olfersii* snakebite patient might present with local symptoms that mimic *Bothrops jararaca* envenomation. It is noteworthy that it is nearly impossible to establish an accurate and safe differential diagnosis without identifying the snakes and detecting any coagulopathy caused by envenomation, especially in settings where the WBCT20 is the only available coagulation test.
14.	Seifert et al. (2011)	USA	Retrospective study	*Crotalinae*	With late effect 11 samples, Without late effect 49 samples	With late effects: 33.8 (1.3–73) Without late effects: 36.4 (1.5–75)	With late effects Male: 7 Female: 4 Without late effects Male: 34 Female: 15	One case demonstrated an INR of >3, a PTT of >60 seconds, and an undetectable fibrinogen level. There were no other cases with severe elevations in INR or PTT. Nevertheless, four cases indicated the onset of hematologic abnormalities that developed late: two with hypofibrinogenemia and two with thrombocytopenia. Both cases of late-onset hypofibrinogenemia were associated with positive D-dimer within the first 48 hours post-envenomation. There was a single case of a prolonged PTT that developed later in life. However, this occurred in a patient who had early hypofibrinogenemia and an elevated D-dimer concentration. Upon discharge, five other patients exhibited fibrinogen or platelet abnormalities that did not persist four or more days post-envenomation. No patient experienced clinically significant bleeding due to a hematologic abnormality.

Legends: PT=prothrombin time; APTT=activated partial thromboplastin time; TAT=thrombin–antithrombin; FDP=fibrinogen degeneration products; INR=international normalized ratio; VICC=venom-induced consumption coagulopathy; WBCT20=20-minute whole blood clotting test; vWF=von Willebrand factor; TT=thrombin time; FBG=fasting blood glucose; AT III=antithrombin III; DIC=disseminated intravascular coagulation.

Strength and limitations

This systematic review offers the advantage of comprehensively examining various aspects of hematologic abnormalities in snakebite, with a specific focus on VICC. However, this systematic review was not conducted with a meta-analysis, which could have enriched the findings of this study.

CONCLUSION

Different types of snakebites have different effects on the hemocoagulation status of patients. Increases in prothrombin time (PT) and activated partial thromboplastin time (APTT) are commonly observed in cases of snakebites. However, the laboratory examination suggests that this may not be accurate for all cases of snakebites. Additionally, the 20-minute whole blood clotting test (WBCT20) may not detect certain types of snakebite.

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Conflict of interest

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Author contribution

RP contributed to the conception and design, analysis and interpretation of the data, and drafting of the article. YH contributed to the drafting of the article, critical revision of the article for important intellectual content, and final approval of the article.

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