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Hemodynamic Effects of Viperidae and Elapidae Snake Bites: A Comprehensive Review

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Abstract

Snakebite is a health issue frequently overlooked in tropical and subtropical countries. Despite snake bites from the families of Viperidae and Elapidae have been reported, there is limited information on the range of clinical manifestations on hemodynamics in adults. This study aims to describe the clinical manifestations of hemodynamic disorders in adults due to snake bites from the Viperidae and Elapidae families. The data for the literature review on hemodynamic disorders caused by Viperidae and Elapidae snake bites in adults was collected through a systematic search on Sciencedirect and PubMed from 2018 to 2023, along with manual searches on Google Scholar. This literature review was conducted using a systematic search on ScienceDirect and PubMed from 2018 to 2023 and a manual search on Google Scholar. The findings were 21,431 snakebite cases from 47 published research studies successfully acquired in this study. There are 36% of coagulopathy cases worldwide, 2% of internal bleeding cases, 25% of arrhythmia cases, and 21% of cardiomyopathy cases. The majority of the cases (70%) were Viperidae bite cases, with some (20%) being Viperidae and Elapidae bite cases and a tiny number (10%) being Elapidae bite cases. The study underscores the importance of a comprehensive approach to snakebite management based on a thorough understanding of the hemodynamic effects induced by these snake families.

Keywords: Elapidae, Hemodynamic, Snake bites, Viperidae

1. Introduction

Snakebite become an epidemic globally includes the World Health Organization (WHO) ignored tropical diseases in 2017[1]. According to WHO, 5.4 million people are bitten by snakes each year, with 2.7 million of those being poisonous snake bites, which cause almost 100,000 fatalities and 400,000 people to be permanently disabled[2]. Only regional reports provide national epidemiological statistics on snakebite cases. Snake venom is a complex mixture of proteins and enzymes that cause complications ranging from

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local to potentially fatal systemic[3]. Pain, swelling, bruising, blistering, and local necrosis are among the local complications of rattlesnake bites. Meanwhile, systemic complications might include acute kidney failure, rhabdomyolysis, stroke, coagulopathy, thrombocytopenia, cardiotoxicity, neurotoxicity, and chemotoxicity[4,5]. A vital aspect of snakebite poisoning that requires consideration is its impact on hemodynamics[6]. Hemodynamic alterations caused by snakebites encompass a wide range of physiological changes, such as systemic effects on blood pressure, heart rate, vascular resistance, and clotting of the blood[7,8]. These changes can present themselves in a variety of ways, influencing vital organ perfusion, tissue oxygenation, and overall patient outcomes[9].

Cardiotoxicity and chemotoxicity from snake venom may trigger rare hemodynamic complications, but they can be fatal if not diagnosed and treated immediately[4,10]. Hypotension, arrhythmias, changes in the electrocardiogram, particularly changes in the ST segment and T waves, Atrioventricular block (AV block), and myocardial infarction are several instances of hemodynamic complications[11]. Snake venom directly impacting the myocardium, hypovolemic shock due to increased vascular permeability, hypercoagulable state leading to vascular thrombosis, and vasospasm are all causes of hemodynamic complications[2,12].

In general, research on the hemodynamic effects of snake bites has not addressed specific familial cases, instead focusing on hemodynamic disorders. This is expected to happen due to the difficulty in obtaining the necessary data to synthesize into a more focused discussion. A comprehensive understanding of the hemodynamic effects induced by Viperidae and Elapidae bites, as well as the clinical implications that arise as a result, has not been completely made available in scientific articles such as Liblik, Garcia-Espinosa[5] which do not address the distinctive characteristics of bite cases among various snake families. It is intended that demonstrating the hemodynamic changes generated by the bite of the Viperidae and Elapidae families could pave the way for a more comprehensive approach to snakebite management, thereby minimizing the burden of this worldwide health concern. The purpose of this literature review was to identify the clinical manifestations of hemodynamic disturbances produced by snake bites coming from the families Viperidae and Elapidae in adults.

2. Material and Method

A systematic search in ScienceDirect and PubMed from 2018 to 2023 was conducted to find data from research examining clinical manifestations of snake bites in people that provide information regarding the impacts of snake bites on hemodynamics[13]. The keywords used were snakebite, snake venom, snake envenomation, hemodynamic, cardiotoxicity, and haemotoxicity. The search was also supplemented with the snowball search method, manual literature review search, and Google Scholar. Hemodynamics is characterized by the physical principles that govern blood flow, pressure, and resistance in the cardiovascular system, which includes the heart, blood vessels, and blood[14,15]. Blood flow, blood pressure, resistance, cardiac output, and vascular conditions are examples of hemodynamic disorders mentioned in the study. The article's relevance is assessed based on the chosen topic of the effect of snake bites on hemodynamics rather than treatment or trials of anti-venom chemicals.

Articles in English or articles with English abstracts were reviewed and selected to acquire data on hemodynamic disorders caused by Viperidae and Elapidae snake bites. The following information was extracted from chosen scientific articles to characterize the hemodynamic effect of snake bites: reference, patient, type of study, country, snake species, and hemodynamic effects. The collected data was grouped in a table and categorized based on the hemodynamic effects resulting from an Elapidae snake's bite. Discussion and consensus were used to adjust disparities between search results. The retrieved variables are as follows: reference, patient, type of study, country, snake species, and results[16,17]. After the data is extracted, it is evaluated with descriptive analysis, to sum up and provide specific information about the study topic's characteristics, patterns, and trends. The analysis results are interpreted to comprehend the significance and implications of the findings discovered. This interpretation entails evaluating the derived descriptive statistics, relating them to the research context, and explaining the significance of any significant findings.

3. Results and Discussion

The initial search yielded 2,770 distinct publications, and the research for the last 5 years yielded 1,070 publications. Forty-seven publications total, from the ones gathered, were used in this literature review. These

Table 1. The study of snakebite clinical manifestations from the Viperidae and Elapidae families for the hemodynamic disorder

No	References	Research type	Samples	Countries	Species of Snake	Results
1	Al Quaiay *et al.*[18]	Case Report	Women aged 70	Sudan	*Vipera berus*	Cardiomyopathy; Coagulopathy
2	Alcoba *et al.*[19]	Cross-sectional study	66 cases	India	Russell's viper; Krait; Cobra snake	Coagulopathy (20); Deceased (2)
3	Anand *et al.*[20]	Prospective Study	300 cases	India	Viperidae snake; Elapidae snake	Coagulopathy (110); Internal Bleeding (7); Deceased (13)
4	Bernelli *et al.*[21]	Case Report	Man. aged 60	Italia	European snake (Vipera Aspis Francisciredi)	Cardiomyopathy
5	Blumenthal *et al.*[22]	Case Report	Man, aged 27	Afrika Selatan	Black mamba (*Dendroaspis polylepis*)	Cardiomyopathy; Deceased
6	Cao *et al.*[23]	Case Report	Man, aged 51	USA	North American Pit viper	Arrhythmia; Coagulopathy
7	Gopala krishnan *et al.*[24]	Retrospective study	185 cases	India	Russell's viper (Daboia russelii); Hump-nosed pit viper (*Hypnale hypnale*)	Coagulopathy (15); Deceased (1)
8	Costa *et al.*[25]	Retrospective Study	92 cases	Brazil	*Bothrops atrox*	Arrhythmia (5); Coagulopathy (69)
9	Ehelepola *et al.*[26]	Case Report	Woman, aged 47	Sri Lanka	Hump-nosed Pit viper	Cardiomyopathy
10	Esiéné *et al.*[27]	Case report	Woman, aged 47	Cameroon	*Echis occellatus* viper	Coagulopathy; Arrhythmia; Deceased
11	Ganesh *et al.*[28]	Case Report	Man, aged 49	India	Russell's viper	Cardiomyopathy
12	George *et al.*[29]	Retrospective study	866 cases	India	Daboia russelii (Western Russell's viper); *Echis carinatus* (Saw-scaled Viper); Naja naja (Spectacled Cobra); *Bungarus caeruleus* (Common Krait)	Coagulopathy (459); Deceased (14)
13	Kelly and Gerardo[30]	Case Report	Man, aged 56	USA	Copperhead snake	Arrhythmia
14	John Binu *et al.*[31]	Retrospective study	34 cases	India	Russell's viper (*D. russelii*); Common cobra (*N. naja*); Krait (*B. Caeruleus*, *Echis carinatus*)	Cardiomyopathy (27); Deceased (2)
15	Johnston *et al.*[32]	Retrospective study	935 cases	Australia	*Notechis scutatus; Pseudechis porphyriacus; Pseudechis australis; Tropidechis carinatus; Pseudechis colletti*; Pseudonaja; Acanthophis spp.; Hydrophiinae	Cardiomyopathy (37)

Table 1. Continued...

No	References	Research type	Samples	Countries	Species of Snake	Results
16	Kumar *et al.*[33]	Cross-sectional study	60 cases	India	Russell's viper; Krait; Cobra snake	Coagulopathy (21); Deceased (8)
17	Li *et al.*[5]	Case Report	Woman, aged 74	China	*Trimeresurus stejnegeri*	Cardiomyopathy
18	Mahendra *et al.*[34]	Prospective Study	45 cases	India	Viper snake; Krait (*Bungarus caeruleus*)	Arrhythmia (3); Coagulopathy (14); Deceased (3)
19	Mana *et al.*[35]	Retrospective study	1160 cases	India	Cobra (Naja naja); Common krait (*Bungarus caeruleus*); Russell's viper (*Daboia russelii*); Saw-scaled viper (*Echis carinatus*)	Coagulopathy (63)
20	Mohan *et al.*[36]	Retrospective Study	150 cases	India	Viperidae snake	Coagulopathy (114); Cardiomyopathy (3)
21	Natarajan[37]	Prospective Study	48 cases	India	Viper snake	Arrhythmia (33)
22	Obeidat *et al.*[38]	Case report	Man, aged 50	Jordan	Arabian Saw-Scaled Viper (*Echis coloratus*)	Coagulopathy
23	Costal-Oliveira *et al.*[39]	Cross-sectional study	412 cases	Brazil	Bothrops snake	Coagulopathy (276)
24	Oliveira *et al.*[40]	Retrospective study	165 cases	Brazil	Bothrops snake; Lachesis snake; Micrurus snake	Coagulopathy (13)
25	Oliveira *et al.*[41]	Prospective Study	100 cases	Brazil	Bothrops atrox	Coagulopathy (40)
26	Ongprakobkul *et al.*[42]	Case Report	Man, aged 52 Woman, aged 46	Thailand	Russell's viper (*Daboia siamensis*)	Man, aged 52: Cardiomyopathy Woman, aged 46: Arrhythmia
27	Srinath *et al.*[43]	Case Report	Man, aged 50	India	Russell's viper	Arrhythmia; Coagulopathy
28	Pecchio *et al.*[44]	Retrospective study	390 cases	Panama	Bothrops snake; Lachesis snake; Micrurus snake	Coagulopathy (199); Arrhythmia (1)
29	Priyankara *et al.*[45]	Case Report	Man, aged 68	Sri Lanka	Cobra (*Naja naja*)	Cardiomyopathy; Arrhythmia
30	Xie *et al.*[46]	Prospective Study	43 cases	Taiwan	*Trimeresurus stejnegeri* stejnegeri	Coagulopathy (43)
31	Laxme *et al.*[47]	Cross-sectional study	127 cases	India	Cobra (*Naja naja*), Russell's viper (*Daboia russelii*), saw-scaled viper (*Echis carinatus*), dan Common krait (*Bungarus caeruleus*)	Coagulopathy (23)
32	Rathnayaka *et al.*[48]	Prospective study	100 cases	Sri Lanka	*Hypnale zara*	Arrhythmia (2); Coagulopathy (1)

Table 1. Continued...

No	References	Research type	Samples	Countries	Species of Snake	Results
33	Reddy[49]	Prospective Study	60 cases	India	Elapid snake; Viper snake	Coagulopathy (15); Cardiomyopathy (5); Arrhythmia (42)
34	Resiere *et al.*[50]	Prospective Study	133 cases	France	*Bothrops atrox*	Coagulopathy (124)
35	Rijal *et al.*[51]	Case report	Woman, aged 25	India	Viperidae snake	Coagulopathy; Arrhythmia
36	Ralph *et al.*[52]	Case report	Man, aged 32	India	Viperidae snake	Arrhythmia; Coagulopathy
37	Varuni *et al.*[53]	Cross-sectional study	100 cases	India	Viper snake; Krait snake; Cobra snake	Arrhythmia (62); Cardiomyopathy (46)
38	Simpson *et al.*[54]	Case Report	Man, aged 73	Columbia	Canebrake rattlesnake (*Crotalus horridus*)	Cardiomyopathy; Arrhythmia
39	Murthy and Rames.[55]	Cross-sectional study	84 cases	India	Viper snake; Krait snake	Cardiomyopathy (8); Arrhythmia (25); Deceased (16)
40	Slade *et al.*[56]	Case Report	Man, aged 62	USA	Northern Pacific rattlesnake	Arrhythmia
41	Kumar *et al.*[57]	Prospective Study	96 cases	India	Cobra (*Naja naja*); Common krait (*Bungarus caeruleus*); Russell's viper (*Daboia russelii*)	Coagulopathy (84); internal bleeding (10); Arrhythmia (28); Cardiomyopathy (22)
42	Tchaou *et al.*[58]	Retrospective study	51 cases	Benin	*E. ocellatus*	Coagulopathy (51); Deceased (2)
43	Thang *et al.*[59]	Cross-sectional study	14.445 cases	Vietnam	Green pit-viper; Cobra snake	Coagulopathy (163)
44	Thein *et al.*[60]	Retrospective study	84 cases	Myanmar	Russel's viper	Coagulopathy (36); Deceased (20)
45	Waitayangkoon *et al.*[61]	Case Report	Man, aged 84	Thailand	Cobra (*Naja siamensis*)	Cardiomyopathy
46	Alfred *et al.*[62]	Retrospective study	948 cases	Myanmar	Russell's viper (*Daboia russeli*); Kobra (*Naja spp.*); Krait (*Bungarus spp.*); Green Pit (*Trimeresurus spp.*)	Coagulopathy (540)
47	Wijewickrama *et al.*[63]	Retrospective study	52 cases	Sri Lanka	*Hypnale spp.*	Coagulopathy (2)

publications cover five continents. The majority of the data are from hospital-based retrospective or prospective epidemiological studies published after 2018 in English. In total, 21,431 snakebite cases were identified in this research. The previous study of snakebite clinical manifestations from the Viperidae and Elapidae families for the hemodynamic disorder can be seen in Table 1.

In this research, a total of 21,431 snake bite cases were successfully obtained. The vast majority of incidents were bites from snakes in the families Viperidae, such

as the Russel's viper, and Elapidae, such as the Common krait. Data regarding the snakes used in the included research and the hemodynamic effects observed by the patients were reported based on these bite cases. There were 83 deaths among the total cases collected, 2,588 cases of coagulopathy, 50 cases of internal bleeding, 183 cases of arrhythmia, and 72 cases of cardiomyopathy. Coagulopathy accounts for 36% of all instances, whereas internal bleeding accounts for 2%, arrhythmia accounts for 25%, and cardiomyopathy accounts for 21% of all cases. The majority of the cases (70%) were Viperidae bite cases, with some (20%) being Viperidae and Elapidae bite cases and a tiny number (10%) being Elapidae bite cases. There were 11 (85%) data cases involving Viperidae snakes and 6 (46%) data cases involving Elapidae snakes among the 13 data cases of patients who died. There were 32 (89%) data cases involving Viperidae snakes and 12 (33%) data cases involving Elapidae snakes among the 36 coagulopathy data cases. There were 16 (91%) Viperidae snake data cases and 6 (27%) Elapidae snake data cases among the 22 Arrhythmia data cases. There were 9 (80%) data cases involving Viperidae snakes and 5 (33%) data cases involving Elapidae snakes among the 15 cardiomyopathy data cases. The majority of the data collected is from the Asian continent, particularly South Asia (24) and India (20 data cases).

3.1 Viperidae and Elapidae

With a total of 35 data cases and 10 data cases combined, bites caused by viperidae form the majority of the data cases discovered. Due to the nature of the snake family, there are more Viperidae data cases predicted than Elapidae data cases[64]. Vipers are typically predators who use camouflage and patience to lure their prey[65]. They normally wait in a hidden place and bite when prey comes within reach. Vipers are known for being more protective and less likely to flee when threatened than other dangerous snakes[66]. When they feel frightened or cornered, they may bite to frighten off possible predators or a perceived threat. Elapidae snakes, on the other hand, are known for their defensive behaviour by intimidating predators or threats[67]. They will only bite as the last option when they detect immediate danger.

Viperidae is a family of venomous snakes known generically as rattlesnakes[68]. Viperidae are identifiable by their strong venom, specialized fangs, and distinctive triangular heads. Viperidae species range in size from less than one meter in length to over two meters in length. They have a wide range of colour patterns and markings that help them blend in with their surroundings. Viperidae have sharp scales, which give their bodies a rough texture. Viperidae features sharp scales on their body, giving them a rough texture. The Viperidae have a pair of long, hollow tusks positioned on the front of their upper jaw. When not in use, these fangs fold flat against the roof of the mouth. Venomous snakes can quickly straighten their fangs when attacking, injecting poison into possible prey or threats. Snake venom is a complex mixture of enzymes, poisons, and proteins that are designed to paralyze and digest their prey while also aiding in defense[69-71]. Venomous snakes are found throughout the world in environments ranging from deserts and prairies to forests and mountains. Europe, Asia, Africa, America, and some regions of the Middle East are home to a variety of Viperidae snake species[72,73]. They have evolved to a variety of climates and habitats, displaying resilience and the ability to thrive in a variety of environments. Viperidae are generally ambush predators, relying on camouflage and speed to catch their prey. They use an organized hunting strategy, waiting for unwary animals to get within striking distance before biting[68]. The variety of snake species can be seen in Figure 1.

Elapidae is a venomous snake family known as elapids[74]. This family comprises some of the world's most well-known and medically significant snakes, including cobras, kraits, mambas, and coral snakes. Elapidae can be identified by their highly neurotoxic venom, hollow tusks, and often slender and elongated bodies. Elapids range in size and appearance from small and thin snakes to larger and more powerful types. Elapidae features smooth scales and a distinguishing pattern, such as stripes, rings, or stripes, with vivid colouration, which serves as a warning signal to possible predators or threats. Elapidae have a pair of fixed hollow tusks on the front of their upper jaw. Their fangs, unlike those of the Viperidae, cannot be folded up against the roof of the mouth. Elapidae, on



(a) **(b)**

Figure 1. **(a)** Trimeresurus macrops, **(b)** Russell's viper. Sources: Wikipedia.

the other hand, maintain their tusks straight, allowing them to deliver venom efficiently when biting their prey or defending themselves. Elapid venom is mostly composed of a strong neurotoxin that attacks the nervous system, causing paralysis and, in severe cases, respiratory failure. Elapids are found in various regions of the world, including Africa, Asia, Australia, and America[75]. They inhabit a wide variety of habitats, including forests, grasslands, deserts, and coastal areas. Several creatures, such as cobras, are adaptable and may live in proximity to human settlements. Elapids have a wide range of hunting habits and strategies. Many elapids are diurnal (active during the day) and are recognized for their agility and speed[76]. The species of snake that are active every day can be seen in Figure 2.

3.2 General Description of Hemodynamic Disorders Due to Snake Bites

Snakebite hemodynamics pertains to the changes in blood circulation and associated factors that occur as a result of a venomous snakebite. When a snake injects its venom into its prey, the venom can have a profound effect on the cardiovascular system, changing blood pressure, heart rate, blood flow, and other hemodynamic parameters[77]. The particular hemodynamic effects of a snakebite might vary based on factors such as the type and amount of venom injected, as well as the individual's response to the venom. There were 83 deaths among the total cases collected, 2,588 cases of coagulopathy, 50 cases of internal bleeding, 183 cases of arrhythmia, and 72 cases of cardiomyopathy. Considering they are related to blood circulation and circulatory system organs, these conditions are classified as hemodynamic disorders.

Snake bites may cause both local and systemic hemodynamic disorders[78]. Local hemodynamic effects may include tissue injury at the area of the snakebite, resulting in edema, inflammation, and impaired blood circulation in the affected area. This can result in tissue necrosis and local ischemia (reduced blood supply). The systemic hemodynamic effects of snake bites can be more severe. Toxin components can cause vasodilation (widening of blood vessels) or vasoconstriction (narrowing of blood vessels), which may affect blood pressure regulation. Toxins found in snake venom affect the heart, causing heart rate changes, rhythm, and contractility. Furthermore, coagulopathy caused by toxins and coagulation disorders might lead to hemodynamic instability. Bleeding can occur when blood coagulation is abnormal, affecting blood volume and circulation. It is necessary to highlight that the severity of hemodynamic disorders caused by snake bites can range from mild changes that resolve spontaneously to major complications that require immediate medical intervention. Proper snake bite management involves monitoring and treating any hemodynamic abnormalities to protect the circulatory system's stability.

3.3 Clinical Manifestations

Coagulopathy is a medical condition characterized by a disruption in the normal blood clotting process following exposure to the venom of certain species of venomous snakes[79]. This is a clinically significant manifestation caused by venom components influencing multiple components of the blood clotting cascade. Clinical symptoms of snake bite coagulopathy include delayed clotting, spontaneous bleeding, bite area bleeding, internal bleeding, and disseminated intravascular coagulation[80]. The total number of coagulopathy cases found in the literature review was 2,588. Coagulopathy was discovered in cases of Viperidae and Elapidae bites, according to the findings of cases of coagulopathy. According to data from Nascimento da Costa, Mota-da-Silva, Colombini[25], there were 69 cases of coagulopathy out of 92 cases of Viperidae bites. Meanwhile, research conducted by Raju, Biju, Mathew[81] states that there were only 23 cases of coagulopathy out of 127 Elapidae bites.

Internal bleeding from a snakebite, also known as hemorrhagic, is a hazardous medical condition that can occur after being exposed to the venom of certain species of venomous snakes. Internal bleeding is defined as the escape of blood from the blood vessels into surrounding tissues or body cavities, which disrupts normal clotting



(a) **(b)**

Figure 2. **(a)** Bungarus caerulus, **(b)** Naja naja. Sources: Wikipedia

mechanisms and has the potential to trigger significant harm to organs and body systems[82]. Internal bleeding symptoms can include bruised patches and bruises, petechiae and purpura, hematomas, hematuria and hematemesis, melena, and hemorrhagic bullae. Internal bleeding caused by snake bites can result in life-threatening complications such as hemorrhagic shock, damaged organs, and Disseminated Intravascular Coagulation (DIC) in extreme cases. There were 50 cases of internal bleeding found in the literature review. It was discovered in cases of Viperidae and Elapidae bites that caused internal bleeding. Natarajan's[83] data revealed that there were 33 cases of internal bleeding out of 48 Viperidae bites. However, the data showed that there were only 10 cases of coagulopathy out of 96 Viperidae and Elapidae bites[2].

There are significant differences in the cases of coagulopathy and internal bleeding in Viperidae and Elapidae bites. The difference in cases of coagulopathy and internal bleeding caused by Viperidae and Elapidae bites can be explained by the venom they contain. The venom that is more dominant in Viperidae is hemotoxin, which contains a protein that inhibits the performance of coagulant factors, making patients bitten by Viperidae susceptible to cases of coagulopathy and internal bleeding. Since Elapidae venom contains more cytotoxic and neurotoxic, the percentage of coagulopathy and internal bleeding cases is lower in Elapidae bites[84].

Arrhythmia resulting from snakebite refers to an irregular heart rhythm caused by venom from venomous snakes. Although cardiac arrhythmias are not as prevalent as other systemic consequences of snake venom, such as neurotoxicity or coagulopathy, they can occur in certain cases and must be diagnosed and treated as soon as possible. Sinus bradycardia, sinus tachycardia, and Atrioventricular (AV) block are all common types of arrhythmias related to snake bites. Snakebite myocardiopathy, also known as snakebite myocardial damage or snakebite cardiomyopathy, is caused by a poisonous snakebite to the heart muscle. Venomous snakes can have a direct harmful effect on the heart when they inject their venom into a victim, causing cardiac dysfunction and damage. Myocardiopathy caused by snake bites can manifest in a variety of ways, including cardiac dysfunction, heart failure, and electrocardiographic abnormalities[85]. There were 255 cases of cardiopathy found in the literature review. Based on the results of cardiopathy cases caused by Viperidae and Elapidae bites. Sunil, Joseph, Varghese[2] discovered 28 cases of arrhythmia and 22 cases of myocardiopathy among 96 cases of Viperidae and Elapidae bites.

The influence of cytotoxins from the two snake families can cause heart problems following Viperidae and Elapidae bites. Viperidae has cytotoxins that disrupt organ function by damaging the cells that come into contact with the poison. Poisoning from Viperidae bites is expected to induce heart problems since the toxin enters the heart area and damages heart function, causing changes in the patient's heart function parameters. Elapidae contains cytotoxic poisons and is accompanied by neurotoxins, both of which can interfere with the function of vital organs. Elapidae poisoning is expected to interfere with heart function by releasing cytotoxic poisons that harm the heart muscle and neurotoxins that weaken the heart muscle.

3.4 Pathophysiological Mechanisms of Hemodynamics

Snakebite poisoning occurs when a person is exposed to venom that contains a variety of biological chemicals, some of which disrupt physiological systems. Some of these components have a direct impact on biological processes such as coagulation, blood pressure regulation, inflammation, nerve function, and muscular impulses. Every venomous snake family has reported Cardiovascular (CV) implications for snakebite poisoning. The pathophysiology of CV involvement has yet to be completely discovered[4]. The example of a snake biting a human can be seen in Figure 3.

The mechanisms underlying snake bite coagulopathy are complex and might differ based on the species of snake along with the structure of their venom. The toxin can target either clotting factors, platelets, or endothelium, resulting in a cascading reaction that alters the blood's coagulation balance. The coagulopathic action of venom is most commonly found in snakes of the families Viperidae (viper) and Elapidae (elapid). These snakes release venom that contains a variety of toxins that may interfere with various phases of the coagulation process, resulting in irregular blood clotting. Snake venom coagulopathy mimics Disseminated Intravascular Coagulopathy (DIC) and may result in severe bleeding and hypovolemic shock. Furthermore, snake venom metalloproteinases destroy cell junctions, weakening blood vessel walls and increasing vascular permeability[86].

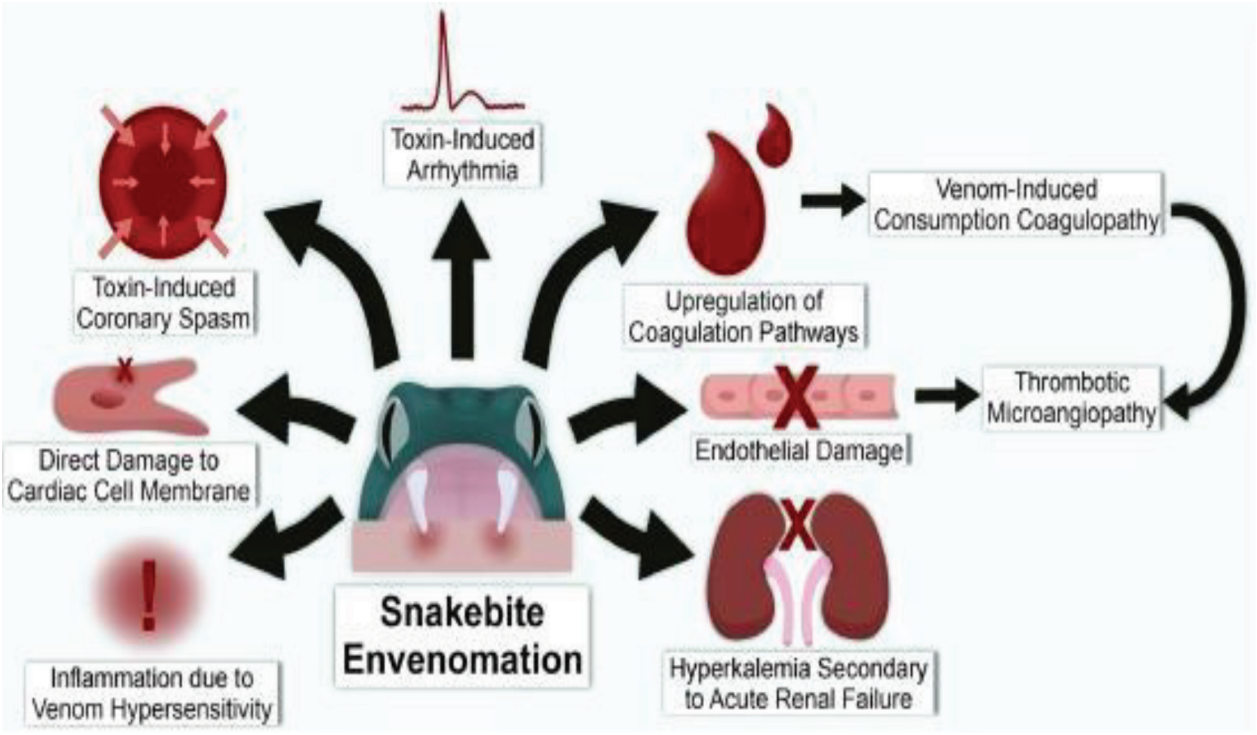


Figure 3. Illustration of snakebite envenomation[4].

When venom is injected into the bloodstream from a snakebite, it can contain a variety of components that alter blood clotting and the functioning of blood vessels. As part of the capillary leak syndrome, haemorrhage in snake venom increases vascular permeability and produces bleeding tendencies. Procoagulants found in snake venom, such as arginine ester hydrolase, can cause hypercoagulability. Hyper-rigidity and hypercoagulability are also produced by hemoconcentration due to hypovolemia caused by haemorrhage. All of these conditions have the potential to cause DIC. Acute myocardial infarction following a Russell viper snake bite, and it is believed that the primary coagulant mechanism may trigger coronary thrombosis, resulting in myocardial infarction[87]. Some snake venoms, particularly those from the viper family (Viperidae), contain enzymes identified as metalloproteinases and serine proteases. These enzymes can disrupt the normal clotting process by degrading blood clotting proteins, including fibrinogen and clotting factors or by activating factors that cause bleeding.

The precise mechanism through which snake venom generates arrhythmia varies based on the species of snake and the composition of their venom. However, various causes, including direct cardiac toxicity, autonomic dysfunction, and systemic effects, may contribute to the development of arrhythmia after snakebite. There is an extensive amount of information available on cardiotoxicity and electrocardiographic changes caused by snake venom exposure. Non-specific ST-T wave abnormalities are the most prevalent electrocardiographic changes following exposure, but further changes such as sinus arrhythmia, atrioventricular block, and sinus bradycardia have been reported as well. After a snakebite, ischemic events such as heart attack (Myocardial Infarction/MI) and stroke are extremely rare. The mechanism by which acute blood clot development is predicted is caused by the activation of the coagulation cascade and cardiotoxicity mediated by proteolytic enzymes and phospholipases in snake venom[88].

Toxins found in some snake venoms can directly impact cardiac tissue, producing anomalies in the heart's electrical conduction system. Cardiotoxins are the second most common type of three-finger toxins. Given its ability to produce lysis in numerous cell types, cardiotoxin is also known as cytotoxin. Cardiotoxins are known for their capacity to disrupt membranes, and the amount to which these peptides can disrupt membranes is dependent on the existence of Ser30 or Pro 28 residues in Circle II[89].

These toxins can affect the electrolyte balance involved in regular heart function or interfere with ion channels. Snake

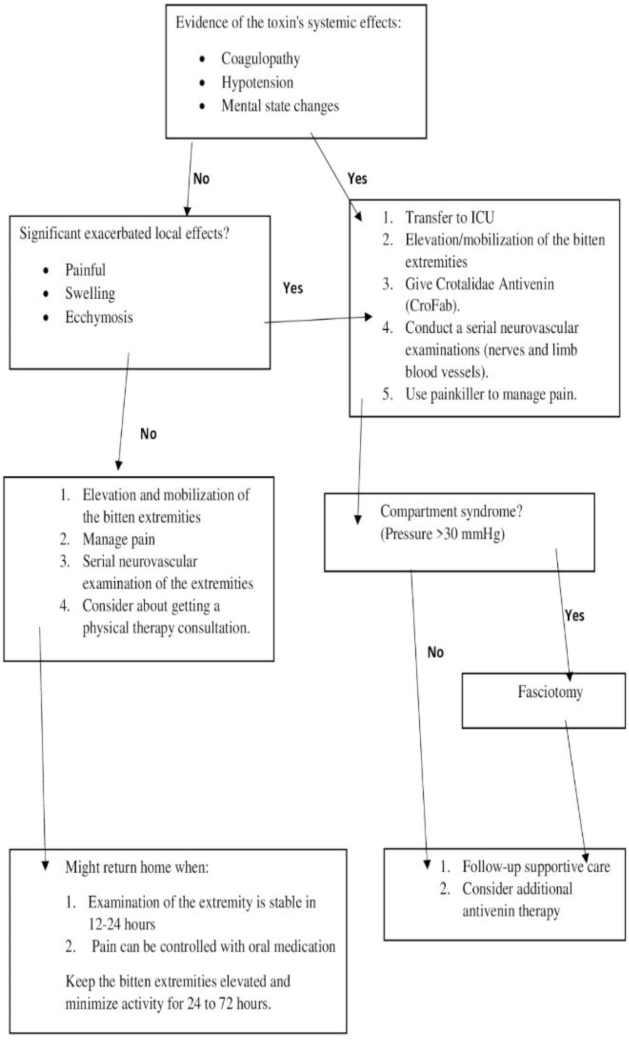


Figure 4. Algorithm for snake bite management.

venom may interfere with the autonomic nervous system, which controls heart rate and rhythm. Arrhythmias can be caused by an imbalance of sympathetic and parasympathetic impulses in the heart. Severe snake bites can result in systemic effects such as hypoxia (low oxygen level) or hypotension (low blood pressure), which can contribute to cardiac rhythm disorders indirectly. The venom of numerous snake species, including viperids (Viperidae) and elapids (Elapidae), can induce myocardiopathy. Toxins found in venom, such as cardiotoxins and myotoxins, may affect cardiac muscle cells directly, producing structural and functional changes.

3.5 Management and Treatment

As hyperdynamic conditions might hasten the spread of snake venom, the patient must be calmed and comforted. The injured area must be immobilized and immediately sent to the hospital for treatment. Avoid incisions, sucking bite wounds, heating, and using a tourniquet. Tourniquets may aggravate existing local necrosis. For bites from snakes in the Elapidae family that elicit neurotoxic effects but no signs of localized edema, Pressure Bandaging and Immobilization (PBI) is indicated. It is not, however, indicated for snake bites from the Viperidae family. PBI use may raise the possibility of more severe local injury[90].

The ABCDE approach (Airway, Breathing, Circulation, Disability and Exposure History) is always prioritized in the hospital, followed by monitoring for hemodynamic signs and symptoms of snake venom spread. The anatomical location of a snakebite is critical to the patient, particularly when it involves vital parts like the head and neck, where it can cause major problems like respiratory blockage, haemorrhage, or death. It is possible to give anti-tetanus vaccinations, antibiotics, and pain relievers. The WHO advises using the pain-killer paracetamol (Acetaminophen) (adult dose of 500 mg to 1 g, maximum 4 g in 24 hrs; children 10-15 mg/kg). Ketamine, apart from paracetamol, is safe enough to be given to patients[91]. The Algorithm for snake bite management can be seen in Figure 4.

If paracetamol or ketamine do not relieve pain, taking an opioid is recommended over Nonsteroidal Anti-Inflammatory Medicines (NSAIDs) due to the risk of bleeding, which can aggravate clotting disorders and thrombocytopenia. Previous research has found no bleeding following Copperhead snake bites treated with NSAIDs; nevertheless, Copperhead bites alone rarely cause clotting disorders. As a result, in general, NSAIDs should be avoided in snakebite situations. The next most critical treatment measure is determining to see if the patient needs anti-venom[92,93].

In general, the anti-venom or anti-venom serum is recommended for snakebites that cause systemic symptoms as well as local symptoms such as swelling, edema, and skin lesions involving the bite site's two major joints. There is only one type of anti-venom available in Indonesia, namely Polyvalent Snake Anti-Venom Serum[94], which is effective against bites from cobra snakes (*Naja sputatrix*), striped snakes (*Bungarus fasciatus*), and ground snakes (*Agkistrodon rhodostoma*)[95]. To avoid complications, anti-venom should be provided within 4 hrs of the bite. However, delays in providing anti-venom have been reported to have positive results. Thus, anti-venom should be provided as long as the indications

are met. Even for Viperidae snake bites, anti-venom medication for up to 24 hrs has been shown to be effective in treating coagulation disorders[84].

Anti-venom can be given intravenously, either as a slow bolus or as a drip infusion. When injected intramuscularly, it has a low bioavailability. Anti-venom can be given Intraosseous (IO) to patients in a situation of emergency. Since the amount of snake venom that enters the body in one bite is the same for children and adults, the dosage is the same. In Indonesia, the suggested dose is 2 vials of Polyvalent Snake Anti-Venom Serum (10 ml) diluted in 100 ml of 0.9% NaCl and then given via drip infusion for 30 min, and the anti-venom can be given every 6-8 hrs. Allergic responses to anti-venom have been observed in 2-50 % of cases and occur immediately after anti-venom. As a result, emergency medicine and resuscitation procedures must be planned ahead of time. The main and most significant treatment for anaphylaxis is epinephrine, which is administered at a dose of 0.01 mg/kg body weight with a maximum dose of 0.5 mg Intramuscularly (IM). If there is no response, repeat the epinephrine dose every 5-15 min. For severe allergic reactions, diphenhydramine at a dose of 1 mg/kg body weight (maximum 50 mg, given slowly over 5 min) or hydrocortisone at a dose of 2 mg/kg body weight given Intravenously (IV) may be considered[92,96].

4. Conclusions

Poisoning from snake bites of the Viperidae and Elapidae families can cause hemodynamic effects that can lead to mortality. Coagulopathy, internal bleeding, arrhythmia, and myocarditis have all been reported as hemodynamic disorders caused by Viperidae and Elapidae bites. The distinction between Viperidae and Elapidae bite cases is due to differences in venom. Elapidae contains neurotoxic poison, and Viperidae contains hemotoxin poison. Snakebite therapy should be considered to prevent complications caused by Viperidae and Elapidae venom.

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6. References

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