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Renal Toxicity in Snakebite Envenomation: Insights into Pathophysiology, Risk Factors, and Management Strategies

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Abstract

Renal toxicity is one of the most severe complications associated with snakebite envenomation, contributing significantly to morbidity and mortality among affected individuals. This review provides a comprehensive analysis of renal toxicity in snakebite victims, focusing on the underlying pathophysiological mechanisms, risk factors, and current management strategies. Snake venom-induced renal damage may occur through various mechanisms, including direct nephrotoxicity, rhabdomyolysis, and coagulopathy. The extent of renal injury is influenced by factors such as venom composition, dosage, route of entry, and the victim's pre-existing health conditions. We also conducted a bibliometric analysis of research trends in this field, highlighting a growing body of literature that reflects increased awareness of snakebite-associated renal complications and advancements in research methodologies. This review synthesizes current knowledge on the prevention and treatment of venom-induced renal toxicity, emphasizing the importance of early intervention, supportive care, and appropriate antivenom therapy. Furthermore, it identifies gaps in existing research and proposes future directions to enhance the understanding and management of renal complications caused by snake envenomation. These insights aim to improve patient outcomes and inform clinical practices in regions with a high prevalence of snakebite envenomation.

Keywords: *acute kidney injury; antivenom therapy; renal toxicity; snakebite envenomation; venom nephrotoxicity*

1. Introduction

Snakebite envenomation represents a major global health burden, particularly in tropical and subtropical regions where venomous snakes are endemic and rural populations face a greater risk of exposure (Afroz et al., 2024; Kasturiratne et al., 2008; Sofyantoro et al., 2022). Worldwide estimates suggest over 421,000 envenomations and 20,000 deaths annually, with the highest burden observed in South Asia, Southeast Asia, and sub-Saharan Africa (Kasturiratne et al., 2008). In recognition of its disproportionate impact on impoverished communities, the World Health Organization (WHO) has designated snakebite envenomation as a neglected tropical disease (Gutiérrez et al., 2017a).

Across multiple regions, including the Caribbean, the Brazilian Amazon, and Sri Lanka, various systemic challenges impede access to lifesaving antivenom therapy. These include long distances to healthcare facilities, insufficient healthcare coverage, and widespread reliance on traditional remedies (Resiere et al., 2018; Maciel Salazar et al., 2021). In sub-Saharan Africa and parts of Asia, persistent antivenom shortages, inadequate

healthcare infrastructure, and delays in medical response further contribute to high morbidity and mortality (Gutiérrez et al., 2014; Patra, & Mukherjee, 2021). Only 8% of hospital pharmacies in Rwanda reportedly stock antivenoms, which are often incompatible with local snake species (Nduwayezu et al., 2020). Similarly, in rural north-eastern Nigeria, reliance on traditional first aid and limited medical access worsens patient outcomes (Iliyasu et al., 2015). Inadequate training among healthcare professionals remains a significant barrier to effective treatment, as evidenced by high rates of inappropriate antivenom use and associated fatalities in India (Gajbhiye et al., 2023). Consequently, these systemic obstacles, ranging from resource limitations to educational gaps, compound the impact of envenomation in low-resource settings (Afroz et al., 2023).

Among the diverse clinical complications, acute kidney injury (AKI) is consistently recognized as one of the most severe and life-threatening consequences of snakebite envenomation. Incidence rates of AKI after snakebite are reported approximately 30–38%, with mortality rates reaching up to 21.5% in adults and 4.4% in children (Bhuvaneshwari & Umarani, 2022; Islam et al., 2020; Priyamvada et al., 2020). Long-term impacts are substantial, as nearly one-third of survivors develop chronic kidney disease (CKD) or hypertension, which adversely affects their quality of life (Priyamvada et al., 2020; Pechprasarn et al., 2025). Several snake species are well-documented causes of nephrotoxicity, particularly those producing hemotoxic or myotoxic venoms. In Asia, *Daboia russelii*, *Daboia siamensis*, *Echis carinatus*, *Hypnale hypnale*, and *Trimeresurus albolabris* are frequently implicated in snakebite-induced renal injury. *D. russelii* is especially notorious for causing AKI and is responsible for a significant proportion of snakebite deaths in regions like Sri Lanka and Southeast Asia (Chaisakul et al., 2019; Kanjanabuch & Sitprija, 2008; Rathnayaka et al., 2021). Additionally, the *Bothrops* genus is a leading cause of nephrotoxicity in Latin America, where it is the most common pit viper encountered (Albuquerque et al., 2019a). These species are not only highly nephrotoxic but are also among the most commonly encountered venomous snakes in their respective regions, making them a major public health concern (Chaisakul et al., 2019; Kanjanabuch & Sitprija, 2008; Rathnayaka et al., 2021).

Among the clinical complications associated with envenomation, renal toxicity is considered one of the most severe and life-threatening outcomes (Priyamvada et al., 2020). Kidney injury may occur through several mechanisms, including direct nephrotoxicity, rhabdomyolysis, and coagulopathy (Chaisakul et al., 2021). Compared to other systemic complications of envenomation, AKI carries a disproportionately high risk of mortality and long-term disability, particularly in regions lacking timely access to dialysis and critical care. Moreover, venom-induced nephrotoxicity remains less systematically reviewed despite its frequency and profound impact on patient outcomes. Therefore, understanding these pathophysiological pathways is essential for developing timely and effective clinical interventions. This review aims to provide a comprehensive analysis of current knowledge on venom-induced renal toxicity, with a focus on global research trends, mechanistic insights, key risk factors, and current management strategies. By synthesizing existing research, this review also highlights knowledge gaps and justifies prioritizing nephrotoxicity as an underrecognized and critical area of focus, while proposing future research directions to inform evidence-based management and improve clinical outcomes for snakebite victims.

2. Bibliometric Analysis of Renal Toxicity and Snakebite

To assess the scholarly output and research trends in the field, a bibliometric analysis was conducted, focusing on articles related to the impact of snake venom on renal function. The search employed the keywords "snake" AND "venom" AND "(kidney OR renal)" within the “Article Title, Abstract, Keywords” fields of the Scopus database in August 2024. Scopus was selected for its extensive indexing of high-quality, peer-reviewed literature across disciplines while also minimizing the inclusion of predatory journals. A total of 1,473 documents published between 1931 and 2023 were identified, reflecting broad scholarly engagement and increasing global interest in the topic. The majority of publications were original research articles (1,233; 83.7%), followed by reviews (154; 10.5%), with the remainder consisting of letters, book chapters, and other document types. English dominated the publications (1,380 documents; 93.7%), aligning with global scientific communication trends. Other languages, including French, Portuguese, Chinese, and Japanese collectively contributed fewer than 5% of the total publications.

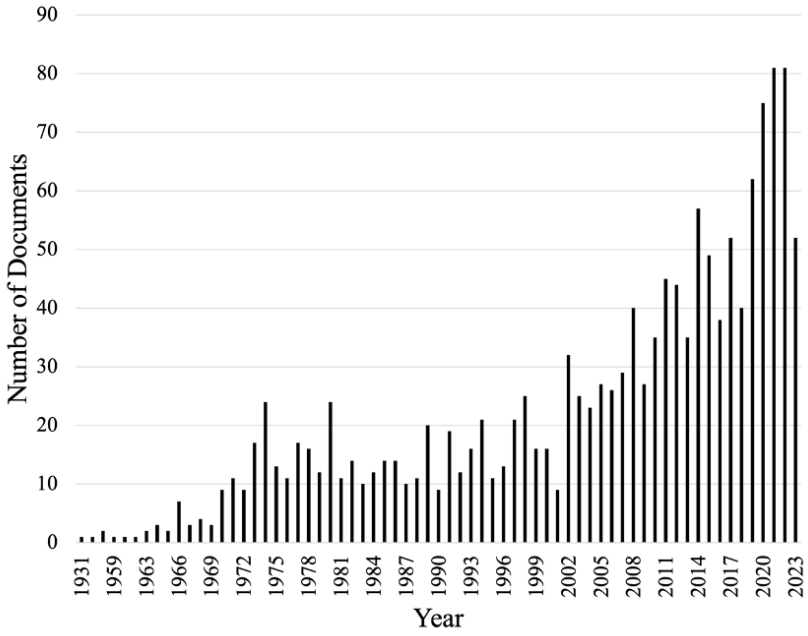


Figure 1 Number of published documents on snake venom and renal function (1931-2023)

Table 1 Top contributing countries to publications on snake venom and renal function

No.	Country	Number of Documents (%)
1	United States	226 (15.34)
2	India	225 (15.27)
3	Brazil	222 (15.07)
4	Australia	106 (7.19)
5	United Kingdom	98 (6.65)
6	Sri Lanka	75 (5.09)
6	Japan	75 (5.09)
7	China	62 (4.20)
8	Germany	51 (3.46)
9	France	49 (3.32)

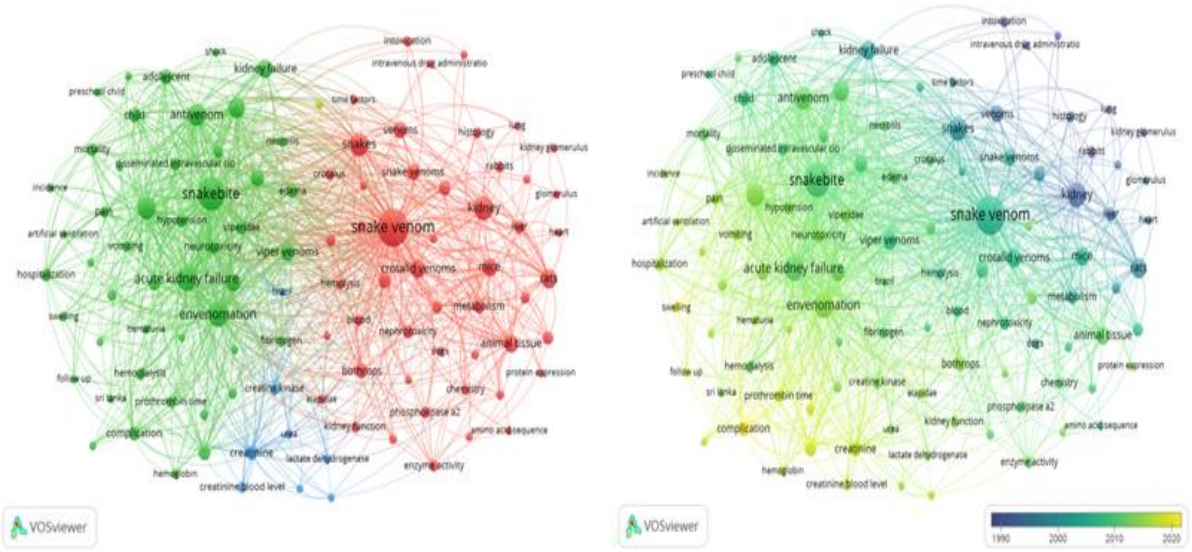
The temporal distribution (Figure 1) reveals a steady increase in publications over time, with peaks in 2021 and 2022 (81 publications each; 5.5%), likely reflecting increased awareness of renal complications, methodological advancements, and enhanced research funding. Recent studies have benefited from improved experimental models (e.g., perfused kidney models, renal cell lines), which have enhancing our understanding of venom nephrotoxicity (Kumar et al., 2022; Villalta et al., 2019).

As shown in Table 1, the United States, India, and Brazil are the leading contributors, collectively accounting for nearly half of the global research output. Other notable contributors include Australia, the United Kingdom, and Sri Lanka, each demonstrating significant publication volumes. This geographic distribution suggests that both the endemic burden of snakebites and the presence of well-established toxinology research infrastructures are key drivers of publication trends.

Institutionally, Brazil stands out, with five institutions in the global top ten, including Universidade de São Paulo, Universidade Federal do Ceará, Instituto Butantan, Universidade Estadual de Campinas, and the Universidade de Costa Rica (Table 2). These institutional patterns underscore Brazil's central role in venom studies, likely due to its high incidence of envenomation and expertise in toxinology (Da Silva et al., 2021). Sri Lanka, the United Kingdom, and Australia also host major research hubs, reflecting regional efforts to better understand and address snakebite-related kidney injury.

Table 2 Top contributing institutions in snake venom and renal function research

No.	Institutions	Country	Number of Documents (%)
1	Universidade de São Paulo	Brazil	48 (3.25)
2	Universidade Federal do Ceará	Brazil	44 (2.98)
2	University of Peradeniya	Sri Lanka	44 (2.98)
3	Instituto Butantan	Brazil	42 (2.85)
4	University of Oxford	United Kingdom	39 (2.64)
5	University of Newcastle	Australia	34 (2.30)
5	Universidade Estadual de Campinas	Brazil	34 (2.30)
6	Universidade Estadual Paulista	Brazil	33 (2.24)
7	Universidad de Costa Rica	Costa Rica	30 (2.03)
8	University of Colombo	Sri Lanka	29 (1.96)



(A) (B)

Figure 2 (A) Network visualization of co-occurrence terms; (B) Overlay visualization of terms co-occurrence. A total of 11,285 keywords were identified with 135 terms occurred at least 50 times. Terms in purple appeared relatively earlier compared to those displayed in yellow

Figure 2 presents a co-occurrence network (Figure 2A) and overlay visualizations (Figure 2B) using VOSviewer, showing that core terms such as "snake venom," "snakebite," "acute kidney failure," and "envenomation" cluster centrally, indicating sustained thematic interest. Earlier studies focused on basic terms like "kidney," "rats," and "intoxication" (purple nodes), whereas recent research trends (yellow nodes) include "acute kidney failure," "hospitalization," and "swelling", indicating a shift toward clinical relevance and patient outcomes. In total, 11,285 keywords were identified, with 135 terms occurring at least 50 times. This extensive keyword network illustrates a highly multidisciplinary research landscape, integrating clinical nephrology, toxinology, pathology, and public health.

In summary, this bibliometric analysis reveals a rapidly expanding body of literature with a strong focus on envenomation-induced renal pathology. The transition from mechanistic animal studies to clinically focused research underscores evolving scientific priorities and growing recognition of snakebite as a serious cause of kidney injury worldwide.

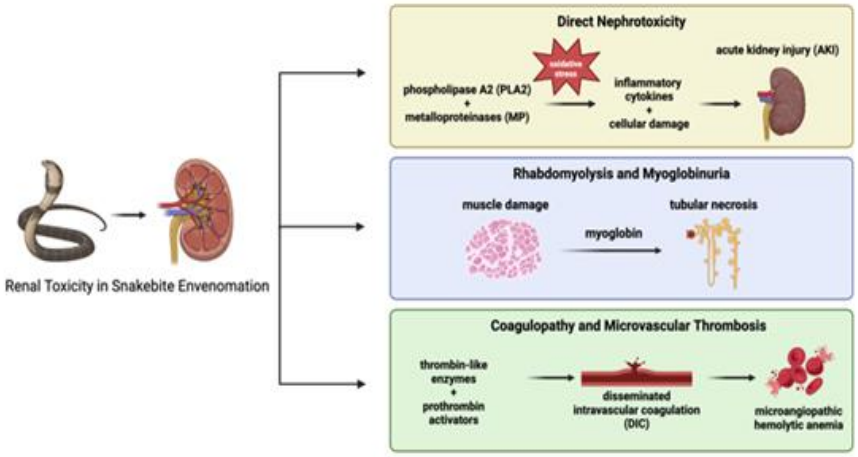


Figure 3 Mechanisms of renal toxicity in snakebite envenomation: (1) direct nephrotoxicity via PLA2 and metalloproteinases causing oxidative stress and AKI, (2) rhabdomyolysis releasing myoglobin leading to tubular obstruction and necrosis, and (3) coagulopathy causing DIC and microvascular thrombosis

3. Pathophysiology of Renal Toxicity in Snakebite

Figure 3 illustrates the three principal mechanisms by which snake venom induces renal toxicity: (1) direct nephrotoxicity, (2) rhabdomyolysis with myoglobinuria, and (3) coagulopathy leading to disseminated intravascular coagulation (DIC) and microvascular thrombosis. These processes collectively contribute to the development of AKI in snakebite victims.

3.1 Direct Nephrotoxicity

The first and most immediate mechanism of venom-induced AKI involves the direct toxic effects of venom enzymes on renal tissues (Figure 3). Snake venom components, particularly phospholipases A2 (PLA2) and snake venom metalloproteinases (SVMPs), can induce cellular injury in both glomerular and tubular compartments. For instance, PLA2 and SVMP fractions from *D. siamensis* venom cause glomerular congestion and tubular epithelial damage, both hallmark features of AKI (Chaisakul et al., 2021). Similarly, Asp-49 and Lys-49 PLA2s from *Bothrops pauloensis* trigger oxidative stress and inflammatory cytokine release, disrupting filtration and reabsorption processes, ultimately leading to glomerular degeneration and atrophy (Marinho et al., 2021). PLA2s and SVMPs also activate endogenous inflammatory and coagulation pathways, further exacerbating tissue damage (Bickler, 2020). Moreover, SVMPs contribute to endothelial disruption, enhancing vascular permeability and promoting inflammatory cascades, while facilitating hemorrhage within the renal microvasculature (Bustillo et al., 2015).

In addition to direct cytotoxicity, envenomation can trigger immune-mediated renal damage, such as glomerulonephritis and interstitial nephritis (Dineshkumar et al., 2018; Rao et al., 2025). These are believed to result from immune complex deposition or delayed-type hypersensitivity reactions to venom antigens. Although relatively rare, such injuries may present subacutely with proteinuria, hematuria, or rising creatinine levels, and can be mistaken for drug-induced or post-infectious nephritis (Dineshkumar et al., 2018; Rao et al., 2025). Clinicians should remain vigilant for these patterns, especially in cases with delayed renal deterioration.

3.2 Rhabdomyolysis and Myoglobinuria

The second mechanism involves venom-induced muscle injury, leading to secondary renal damage (Figure 3). Certain snake venoms contain myotoxic components that cause rhabdomyolysis, resulting in the release myoglobin into circulation. Myoglobin is nephrotoxic and can precipitate within renal tubules, causing obstruction, oxidative damage, and necrosis. Experimental studies have demonstrated that *Pseudechis australis* venom induces muscle fiber necrosis and macrophage infiltration, leading to the formation of myoglobin casts in renal tubules (Azevedo-Marques et al., 1985; Ponraj & Gopalakrishnakone, 1995). Similarly, envenomation by *Crotalus durissus terrificus* results in widespread myonecrosis and elevated serum myoglobin levels, contributing to tubular toxicity (Azevedo-Marques et al., 1985). In clinical settings, particularly in India, myoglobinuria is a recognized contributor to AKI,

often culminating in acute tubular and cortical necrosis (Chugh, 1989). Early identification and management of rhabdomyolysis, through aggressive hydration and urine alkalinization, are critical for preventing irreversible renal damage.

3.3 Coagulopathy and Microvascular Thrombosis

The third mechanism involves hemostatic dysregulation caused by venom-induced coagulopathy, which can impair renal perfusion and lead to ischemic injury (Figure 3). Certain snake venoms contain thrombin-like enzymes and prothrombin activators that induce venom-induced consumption coagulopathy (VICC). Although VICC mimics DIC - manifesting as elevated D-dimer, prolonged clotting times, and reduced fibrinogen - it typically lacks systemic microthrombi and associated organ failure. However, in severe cases, VICC can progress to thrombotic microangiopathy, characterized by AKI, thrombocytopenia, and hemolytic anemia, which may persist beyond the resolution of coagulopathy (Isbister, 2010).

Experimental studies of *Bothrops* venom have shown that Moojenactivase (MooA), a procoagulant metalloprotease, induces depletion of coagulation factors, cytokine upregulation, and leukocytosis, ultimately leading to DIC and glomerular microthrombosis (Sartim et al., 2017). Similarly, envenomation by *Pseudonaja textilis* can cause severe DIC with intense fibrinolysis, impairing capillary flow and leading to renal infarction (Masci et al., 1990). Understanding the interplay between coagulopathy and renal microvascular injury is vital for managing snakebite-induced AKI, particularly when considering antivenom timing, supportive therapies, and early renal replacement strategies.

In addition to microvascular thrombosis, hemodynamic alterations represent an important secondary mechanism of renal injury. Venom-induced systemic bleeding, vascular leakage, and hypotension can significantly reduce renal blood flow, leading to renal ischemia and AKI (Alvitigala et al., 2025; Kanjanabuch & Sitprija, 2008; Sarkar et al., 2021). These hemodynamic disturbances are often compounded by venom-induced coagulopathy, capillary leak syndrome, and hypovolemia, all of which further compromise renal perfusion and oxygenation (Alvitigala et al., 2025; Gutiérrez et al., 2009; Kanjanabuch & Sitprija, 2008). The resulting renal ischemia, along with the direct nephrotoxic effects of venom, contributes to acute tubular necrosis and other forms of kidney damage commonly observed after snakebite (Alvitigala et al., 2025; Kanjanabuch & Sitprija, 2008; Sarkar et al., 2021).

4. Risk Factors for Renal Toxicity in Snakebite Victims

4.1 Snake Species and Venom Composition

Renal toxicity from snake envenomation is a multifaceted condition influenced by the type of snake and the specific biochemical composition of its venom. AKI is commonly reported following bites from *D. siamensis*, where nephrotoxic severity correlates with ontogenic variation in venom composition, particularly the concentrations of PLA2 and SVMPs (Chaisakul et al., 2021; Chaiyabutr et al., 2022). Similarly, the venom of *Hypnale* spp. also leads to AKI, with toxicity levels differing among species (Silva et al., 2012). In *Bothrops* snakes, specific venom components such as SVMPs and LAAOs are directly associated with renal pathogenesis (Albuquerque et al., 2019b). Although primarily neurotoxic, *Micrurus* snake venoms also cause AKI through direct nephrotoxicity and oxidative stress (Braga et al., 2020). These findings highlight the importance of species-level venom profiling to predict renal outcomes and guide appropriate therapeutic interventions.

4.2 Victim's Health Status

The health status of snakebite victims significantly affects their risk of developing venom-induced renal toxicity. Pre-existing conditions such as hypertension, diabetes, and CKD increase susceptibility to AKI post-envenomation. Studies have shown that conditions like hypertension and diabetes exacerbate the risk of AKI following snakebites, necessitating early intervention (Chugh, 1989; Nirja & Rathore, 2020). Patients with advanced stages of CKD, particularly those in stages 3–5, are at higher risk for developing AKI following a snakebite, as these stages are characterized by significantly reduced kidney function and lower resilience to additional renal insults (Herath et al., 2012; Waiddyanatha et al., 2023). CKD can also develop as a long-term consequence of snake envenomation, highlighting the impact of pre-existing renal issues on envenomation outcomes (Waiddyanatha et al., 2019). Factors such as age, dehydration, and overall health further influence the risk of renal toxicity. The risk of snakebite-associated AKI increases with age, with studies showing that patients over 50 years old are particularly vulnerable (Noutsos et al., 2022a). Older patients are more likely to develop AKI, particularly

when dehydration and muscle injury are present (Nirja & Rathore, 2020). Venom from juvenile snakes, which is richer in enzymatic toxins, tends to cause more severe nephrotoxicity, suggesting that both snake and victim age influence renal outcomes (Chaiyabutr et al., 2022). Consequently, these factors underscore the necessity of personalized management strategies in snakebite victims, taking into account their pre-existing health conditions and overall physiological resilience.

4.3 Dosage and Route of Venom Entry

The severity of renal toxicity in snakebite victims is closely tied to the venom dose and the route of entry, both of which significantly influence systemic effects. Higher venom doses amplify nephrotoxic effects due to increased concentrations of harmful components such as phospholipases and metalloproteinases, leading to greater kidney damage. *Bothrops asper* venom administered intramuscularly in mice causes significant renal damage, including tubular necrosis, with severity correlated with venom dosage (Chaves et al., 1992). Similarly, studies on *Aipysurus laevis* and *Bothrops moojeni* venoms have shown that higher doses and intravenous administration lead to pronounced renal damage (Boer-Lima et al., 2002; Ryan & Yong, 2002).

The venom entry route significantly influences systemic toxin distribution (Aphrodita et al., 2025). Venoms injected intravenously distribute faster and cause more severe renal effects compared to intramuscular or subcutaneous routes, which display slower absorption and elimination (Sanhajariya et al., 2018). Additionally, the route of administration significantly affects toxicity, as venoms are less toxic intraperitoneally than intravenously (Oukkache et al., 2014). Furthermore, research on *Naja haje* venom demonstrated that intramuscular injection caused significant renal oxidative stress and histopathological alterations, underscoring the impact of the entry route on renal outcomes (Tohamy et al., 2014). In real-world settings, bites to highly vascularized areas (e.g., face, neck, or upper limbs) may increase the risk of systemic envenomation and subsequent renal complications. However, direct clinical evidence quantifying how bite location influences renal toxicity in humans remains limited. Much of the available data derives from experimental animal models and in vitro studies. Therefore, while data from these studies suggests that more rapid systemic absorption is likely in highly vascular regions, further clinical research is needed to confirm these associations and guide evidence-based management.

4.4 Indirect and Contextual Risk Factors

Beyond venom-specific and host-related determinants, several indirect factors exacerbate renal outcomes following envenomation. Delayed antivenom administration remains a key modifiable risk factor, as prolonged venom circulation increasing the likelihood of AKI and systemic complications (Salah Eldin & Hafez, 2017; Variawa et al., 2021). Inadequate healthcare infrastructure, particularly in rural or underserved areas, limits timely diagnosis and treatment, further compounding renal risk (Hamza et al., 2021; Sharma, 2005). Additionally, secondary infections at the bite site or due to systemic immune suppression can worsen renal inflammation and promote the development of glomerulonephritis or interstitial nephritis (Bonilla-Aldana et al., 2024; Cavalcante et al., 2023). These contextual challenges underscore the critical need for early intervention, strengthened healthcare systems, and improved public awareness to reduce renal morbidity in snakebite victims.

5. Management Strategies

5.1 Immediate First Aid and Pre-Hospital Care

Effective early management of snakebite envenomation is essential to prevent severe complications, including renal toxicity. Initial first aid should prioritize patient stabilization and minimizing venom spread by immobilizing the affected limb with a splint or rigid object, thereby reducing muscle contractions that promote venom dissemination. Pressure immobilization is currently the only evidence-based first aid technique proven to limit venom spread, although it is challenging for laypersons to apply correctly (Avau et al., 2016). Another study highlighted that pressure immobilization bandages and related methods are considered the most effective interventions to delay systemic toxicity from venomous snakebites; however, they may increase local toxicity depending on the venom type (Parker-Cote & Meggs, 2018). Firm pressure combined with limb immobilization has been reported to effectively delay venom spread, emphasizing the critical role of using a splint or rigid object (Engel, 1979). Collectively, these studies highlight the importance of limb immobilization in stabilizing patients and limit venom dissemination in snakebite management.

Traditional first aid measures, such as making incisions, sucking out venom, or applying tourniquets, should be avoided, as they can cause additional harm, increase inflammation, and pose risks of secondary infection. The use of tourniquets has been associated

with increased local toxicity, a higher need for antivenom, longer hospital stays, and a greater risk of wound infections (Parker-Cote & Meggs, 2018). Suction devices, previously believed to be effective, have been shown to be ineffective and may worsen tissue damage, causing necrosis and delaying healing (Bush, 2004). Additionally, methods involving incision and suction, whether performed by mouth or mechanical devices, can cause injuries and infections without effectively removing venom (Bush, 2004). The use of traditional remedies, such as herbal concoctions applied topically or ingested, has also been associated with increased mortality and disability rates, delayed hospital presentation, and higher medical costs (Michael et al., 2011).

5.2 Timely and Appropriate Administration of Antivenom

Antivenom therapy is the cornerstone of snakebite envenomation management, particularly for mitigating renal toxicity. The primary function of antivenom is to neutralize venom toxins, thereby reducing their harmful effects on vital organs, including the kidneys, by facilitating toxin clearance from the bloodstream. For example, the administration of Hemato Polyvalent Antivenom (HPAV) has been shown to significantly mitigate morphological damage to the liver, heart, and kidneys caused by *Calloselasma rhodostoma* venom, underscoring its effectiveness in neutralizing nephrotoxic effects (Khimmaktong et al., 2022; Kusuma et al., 2023).

Timely and appropriate administration of antivenom is crucial, as it is strongly associated with improved outcomes and a reduced risk of AKI. Noutsos et al. (2020) reported that AKI occurred in 94% of thrombotic microangiopathy (TMA) cases following snakebite, highlighting the critical role of early antivenom administration. Furthermore, early administration of antivenom is essential for managing VICC and preventing progression to TMA and AKI (Noutsos et al., 2020). The optimal timing for antivenom administration after snakebite is as early as possible, ideally within the first 1–6 hours after the bite, to maximize effectiveness and reduce complications (Chuang et al., 2021; Houcke et al., 2023; Isbister, 2023, 2024). Early administration, preferably within 1 hour of hospital arrival, has been shown to reduce pain, shorten hospital stays, and accelerate recovery from coagulopathy, while delays can lead to prolonged symptoms and worse outcomes (Chuang et al., 2021; Houcke et al., 2023; Pujo et al., 2025). Research on *Bothrops jararaca* envenomation has demonstrated that antivenom administration significantly improves renal hemodynamics and reduces oxidative stress, thereby attenuating AKI (Gois et al., 2017). A retrospective study of snakebite patients in India found that delays in antivenom therapy were significantly associated with AKI occurrence, emphasizing the importance of timely intervention (Nirja & Rathore, 2020).

The efficacy of antivenom therapy depends on accurate dosing and the route of administration. Intravenous administration is preferred over intramuscular routes due to its superior efficacy in neutralizing venom in both the systemic and lymphatic circulation, which is critical for optimal clinical outcomes (Gamulin et al., 2023). Insufficient dosing may fail to prevent renal damage, whereas excessive dosing increases the risk of adverse reactions. Studies on *D. siamensis* venom have shown that only high doses of monovalent antivenom administered early can prevent venom-induced nephrotoxicity, whereas lower doses are ineffective (Chaisakul et al., 2019). Similarly, a randomized controlled trial in Nepal comparing high versus low initial doses of polyvalent antivenom for neurotoxic envenomation found no significant difference in primary outcomes but highlighted the practical advantage of a single high dose without increased adverse reactions (Alirol et al., 2017). Polyvalent antivenoms have also been shown to effectively neutralize multiple venom types, such as HPAV neutralizing both *H. hypnale* and *D. russelii* venoms, making them particularly useful in regions with diverse venomous species (Chaisakul et al., 2020; Tan et al., 2011). However, the decision between monovalent and polyvalent antivenom should be guided by the specific patient condition and venom characteristics to optimize treatment outcomes and minimize risks (Ratanabanangkoon, 2023).

5.3 Supportive Care

Supportive care for managing renal toxicity due to snake envenomation primarily aims to maintain renal perfusion while preventing fluid overload. Ensuring adequate hydration is essential to prevent AKI (Cai et al., 2020). However, fluid administration must be carefully tailored to the patient's hemodynamic status, urine output, and fluid losses to maintain optimum fluid balance. Intravenous fluids are commonly administered to preserve renal perfusion and prevent AKI, however, fluid overload remains a significant concern as it can lead to organ dysfunction and hinder recovery (Prowle et al., 2012).

Conservative fluid management strategies targeting a neutral or negative fluid balance after initial resuscitation have been shown to reduce AKI incidence and improve outcomes in critically ill patients (Vaara et al., 2021). Additionally, goal-directed therapy (GDT) involving limited fluid resuscitation and inotropic support has been associated with a reduced risk of postoperative AKI (Prowle et al., 2012). It is crucial to individualize fluid therapy based on the patient's specific characteristics and the nature of their acute illness to avoid both hypovolemia and fluid overload. Evidence indicates that fluid overload is linked to higher mortality rates in patients with AKI, underscoring the importance for meticulous fluid management (Zhang et al., 2015). In resource-limited settings, fluid management can be is particularly challenging due to limited availability of infusion pumps, patient monitoring systems, or intravenous fluids. These constraints necessitate the use of simplified clinical assessment tools, such as capillary refill time and urine output, to guide fluid therapy decisions.

In cases of oliguria or fluid retention, diuretics may be employed to promote diuresis and mitigate the risk of fluid overload. However, their use should be carefully tailored to avoid dehydration and worsening renal perfusion. In critically ill patients with AKI, diuretics can help manage fluid overload, but they must be used judiciously to avoid hypovolemia and recurrent renal injury (Prowle et al., 2014). While diuretics are not effective in preventing AKI or improving outcomes once AKI has developed, they may alleviate symptoms of pulmonary edema due to volume overload (Levey & James, 2017). In specific scenarios, such as rhabdomyolysis-induced AKI, diuretics may help eliminate nephrotoxic substances. Continuous venous-venous hemofiltration (CVVH) has been used effectively to remove myoglobin in patients with rhabdomyolysis and AKI who present with oliguria, suggesting a role for forced diuresis in such situations (Zhang et al., 2012). However, the overall role of diuretics in AKI management remains controversial, with some studies indicating potential harm if not carefully administered (Arbel et al., 2019). The use of CVVH, while beneficial in critical care, is rarely available in rural or resource-limited facilities. The cost, need for specialized equipment, and shortage of trained personnel often make renal replacement therapy (RRT) inaccessible in regions most burdened by snakebite. As such, supportive care in these settings often relies on conservative fluid strategies and symptom management rather than renal replacement therapies.

Management of snake venom-induced renal toxicity associated with coagulopathy or DIC centers on early administration of antivenom, which remains the primary intervention to neutralize circulating venom and limit further toxin-mediated damage (Noutsos et al., 2022b; Patil et al., 2019). However, antivenom may not prevent the development of thrombotic microangiopathy (TMA) or fully reverse established coagulopathy, particularly if administered after significant tissue injury has occurred (Noutsos et al., 2022b; Parihar et al., 2023; Patil et al., 2019). Supportive care is critical, including close monitoring of renal function, fluid and electrolyte management, and timely initiation of kidney replacement therapy (dialysis) when indicated (Noutsos et al., 2022b; Sarkar et al., 2021). In cases of severe coagulopathy or active bleeding, transfusion of blood products, such as fresh frozen plasma may be considered to correct clotting factor deficiencies (Patil et al., 2019). Although therapeutic plasma exchange has been attempted in some cases of TMA, current evidence does not support its routine use (Noutsos et al., 2022b; Shankar et al., 2024). Long-term follow-up is recommended due to the increased risk of CKD in survivors (Noutsos et al., 2022b; Sarkar et al., 2021).

5.4 Monitoring and Follow-Up

Managing renal toxicity resulting from snake envenomation necessitates vigilant monitoring and extended follow-up. During the acute phase, frequent assessments of serum creatinine, blood urea nitrogen (BUN), urine output, and electrolytes are crucial (Sarkar et al., 2021). Advanced biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C provide earlier detection of kidney injury than traditional markers. Studies have shown that urinary NGAL and serum cystatin C are more effective than serum creatinine in predicting AKI within hours of envenomation (Ratnayake et al., 2019; Sarkar et al., 2021; Wijewickrama et al., 2021). In *D. russelii* bites, urinary clusterin (uClu), urinary NGAL (uNGAL), and serum cystatin C (sCysC) increase earlier than serum creatinine, indicating their utility for early diagnosis (Ratnayake et al., 2019). Similarly, in cases of envenomation by the *Hypnale* spp., elevated levels of serum cystatin C and urinary NGAL are significant predictors of moderate to severe AKI (Wijewickrama et al., 2021). Despite their diagnostic value, the widespread implementation of NGAL, cystatin C, and other novel biomarkers remains

limited in many low-income settings due to cost and availability. In such cases, clinicians must rely on conventional tests and clinical judgment to monitor renal function. Strengthening laboratory capacity and promoting cost-effective point-of-care testing are critical priorities for improving snakebite care in these regions. Long-term follow-up is essential, as AKI may progress to CKD, requiring continuous monitoring and management to prevent chronic renal damage (Sarkar et al., 2021).

5.5 Novel Antivenom Strategies and Emerging Therapeutics

The current standard of care for venom-induced toxicity relies primarily on animal-derived polyclonal antivenoms (Gutiérrez et al., 2017b; Silva & Isbister, 2020). While effective in neutralizing systemic toxicity, these preparations have significant limitations, including batch variability, restricted tissue penetration, risk of hypersensitivity reactions, and incomplete neutralization of specific nephrotoxic components (Alangode et al., 2020; Hamza et al., 2021). Recent advancements in antivenom technology have introduced several innovative approaches (Uko et al., 2024), that may address these limitations and improve outcomes in cases of venom-induced AKI.

Recombinant antivenoms, developed through the expression of monoclonal antibodies or antibody fragments in heterologous systems, enable precise targeting of nephrotoxic venom components such as PLA2s and SVMPs (Menzies et al., 2025; Zhu et al., 2025). These agents offer improved specificity, reduced immunogenicity, and enhanced production scalability, characteristics that are particularly valuable for addressing regional venom variations and reducing the risk of adverse reactions (Adams et al., 2024; Khalek et al., 2024; Ledsgaard et al., 2023). Small molecule inhibitors, including varespladib and marimastat, function by directly inhibiting the enzymatic activity of PLA2s and SVMPs, respectively (Albulescu et al., 2020; Knudsen & Laustsen, 2018; Xie et al., 2020). Owing to favorable pharmacokinetic properties and oral bioavailability, small molecule inhibitors are considered promising adjuncts or standalone interventions, particularly in prehospital settings where access to traditional antivenoms is delayed. Human monoclonal antibodies, engineered to exhibit high-affinity binding to venom proteins, represent another class of next-generation therapeutics (Khalek et al., 2024; Ledsgaard et al., 2022, 2023). These antibodies show potential in neutralizing venom-induced coagulopathy and thrombotic microangiopathy, both of which are implicated in the pathogenesis of renal injury. The use of fully human antibody formats minimizes the likelihood of hypersensitivity reactions and improves therapeutic safety profiles (Khalek et al., 2024; Ledsgaard et al., 2023). Synthetic peptides, designed to mimic structural epitopes or functional motifs of venom targets, act as competitive inhibitors of toxin–host interactions (Laustsen et al., 2022; Lentz et al., 1987; Saladini et al., 2024). In the context of renal toxicity, synthetic peptides may prevent the binding of nephrotoxic venom components to glomerular or tubular cell receptors, thereby mitigating cytotoxicity, inflammation, and subsequent fibrosis. Nanobodies, or single-domain antibodies derived from camelid heavy-chain antibodies, possess high thermal and proteolytic stability, strong tissue penetration, and rapid systemic distribution (Alirahimi et al., 2018; Mejri et al., 2024; Wade et al., 2022). These properties make nanobodies particularly suitable for neutralizing low-molecular-weight venom toxins that are rapidly distributed to target organs, including the kidneys. Collectively, these novel antivenom strategies present a transformative shift in the management of snakebite envenomation, with particular relevance for mitigating venom-induced renal injury. The integration of these modalities into clinical practice may improve therapeutic outcomes, reduce antivenom-associated complications, and expand access to effective treatments in underserved populations.

6. Prevention and Public Health Implications

6.1 Education and Awareness

Education and awareness are critical for preventing snakebite-induced renal toxicity, particularly in rural areas. In India, a comprehensive community education program significantly enhanced awareness of snakebites, resulting in faster hospital arrivals and improved first aid practices, which are vital for preventing complications such as renal toxicity (Samuel et al., 2020). The National Snakebite Project in India further illustrates the importance of structured educational initiatives, focusing on capacity building within health systems and community education on snakebite prevention and management, thereby reducing the overall burden of snakebite envenomation (Gajbhiye et al., 2023). These initiatives highlight the essential role of education in mitigating the adverse effects of snakebites, particularly in resource-limited rural settings.

Effective community programs should also address snakebite risks, prevention strategies, and the importance of timely medical care, while actively

countering harmful cultural practices. Research in Myanmar revealed substantial gaps in first aid knowledge despite awareness of snakebite prevention, with many communities relying on harmful practices like tourniquets, emphasizing the need for targeted educational interventions (Mahmood et al., 2019). Similarly, studies in Kenya found prevalent traditional first-aid practices and delays in seeking medical care, underscoring the need for integrated community education and healthcare worker training to improve outcomes (Van Oirschot et al., 2021). In Maharashtra, India, a multi-sectoral approach was recommended to address the widespread use of harmful traditional methods and empower both communities and healthcare workers, aiming to reduce snakebite mortality and morbidity (Chaaithanya et al., 2021). Despite the importance of public education, systemic constraints frequently limit the effectiveness of these initiatives. In many rural settings, antivenom is not only scarce but also unevenly distributed due to fragmented procurement systems and logistical challenges. These supply chain issues delay access to life-saving treatment, thereby exacerbating the risk of complications such as renal toxicity. Addressing these bottlenecks requires coordinated policy-level responses, including centralized stock management, transparent demand forecasting, and government investment in local antivenom production and distribution infrastructure.

Public health campaigns should leverage multiple platforms, such as community outreach and social media, to promote early antivenom use and reduce complications. Social media has proven effective in health communication by rapidly disseminating targeted messages to large audiences, promoting behavior change, and improving health outcomes (Plackett et al., 2020). For example, social media campaigns have successfully influenced health behaviors and promoted cancer screening and early diagnosis, highlighting their potential for enhancing public health interventions (Plackett et al., 2020). However, its utility in the context of snakebite management remains underexplored. A more critical and strategic approach is required, involving community influencers, culturally adapted content, and fact-checking mechanisms to prevent misinformation-especially in regions where social media is the primary source of health information.

Improving access to antivenom and strengthening healthcare worker training are also vital. In Thailand, the establishment of a national antidote program in 2010 significantly improved antivenom availability and utilization by centralizing stocks, optimizing distribution, and training healthcare providers, which also reduced costs and wastage (Suchonwanich & Wananukul, 2018). Similarly, decentralizing antivenom treatment to primary healthcare facilities and training professionals in standardized protocols in the Brazilian Amazon are expected to enhance access and outcomes for indigenous populations facing geographic barriers (Monteiro et al., 2020). In Kenya, healthcare workers expressed a need for training in snakebite management and antivenom administration, highlighting that limited resources and delays in care are major obstacles to effective treatment (Barnes et al., 2021). These examples underscore the global importance of enhancing antivenom access and improving healthcare worker training to mitigate the impact of snakebites. National health policies must prioritize continuous medical education programs and ensure adequate resourcing of rural healthcare facilities to facilitate timely diagnosis and treatment.

6.2 Improvement of Healthcare Infrastructure

Enhancing healthcare infrastructure is essential for mitigating snakebite-induced renal toxicity. Prompt access to antivenom therapy is critical, as delays increase the risk of severe complications such as AKI, a common and serious outcome in critically ill patients associated with poor prognosis and increased mortality (Li et al., 2021). Developing reliable antivenom supply chains and expanding dialysis services, such as satellite centers and mobile units, are crucial for timely patient care. Satellite and mobile dialysis units have proven effective in delivering patient-centered care in rural areas, reducing travel burdens, and improving access to treatment. However, the broader resource constraints that characterize many endemic regions including inadequate cold chain infrastructure, limited diagnostic laboratory capacity, and shortage of trained personnel pose significant barriers to effective snakebite care. These systemic limitations not only hinder antivenom delivery but also contribute to delays in diagnosing and managing complications such as AKI.

Training healthcare providers to recognize early signs of renal impairment and incorporating point-of-care testing can also enhance early detection and management of renal complications. Early treatment and monitoring of symptoms such as oliguria and anuria can prevent the progression of acute renal failure, a frequent complication following envenomation by snakes, particularly those from the Viperidae family (Horo et al., 2022). Biomarkers such

as NGAL have shown promise as early diagnostic indicators for AKI in snakebite victims, facilitating timely decisions regarding RRT (Senthilkumaran et al., 2021). This is crucial since traditional markers, such as serum creatinine, can take up to 48 hours to reflect significant changes, potentially delaying essential interventions (Senthilkumaran et al., 2021). Nevertheless, the application of such biomarkers remains limited in low-resource settings due to their cost, lack of point-of-care platforms, and their exclusion from clinical guidelines. Integrating biomarker use into national snakebite protocols and investing in affordable diagnostic technologies could enhance early detection and improve clinical outcomes.

Comprehensive clinical management, including serial blood tests and neurological evaluations, is also vital for monitoring systemic envenomation and renal impairment in suspected snakebite cases (Isbister et al., 2013). Ultimately, bridging the gap between primary care capabilities and tertiary-level interventions will require targeted policy reforms, including mobile outreach programs, telemedicine integration, and multi-sectoral collaboration.

7. Conclusion

Snakebite envenomation poses a major public health risk, particularly in low-resource tropical regions, with renal toxicity representing one of the most severe complications. This review underscores the complex mechanisms of venom-induced renal damage, including direct nephrotoxicity, rhabdomyolysis, and coagulopathy, highlighting the urgent need for improved management strategies. Key challenges include limited access to effective antivenoms, inadequate healthcare infrastructure, and insufficient training of healthcare professionals. Enhancing early diagnosis, ensuring timely antivenom administration, and strengthening supportive care are crucial steps in mitigating renal damage. Future research should focus on optimizing treatment protocols and exploring novel therapeutic strategies to reduce the impact of snakebite-induced renal toxicity, emphasizing a multidisciplinary approach to improve outcomes for affected populations.

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9. CRediT Statement

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10. References

Adams, A. C., Grav, L. M., Ahmadi, S., Holst Dahl, C., Ljungars, A., Laustsen, A. H., & Nielsen, L. K. (2024). Single-batch expression of an experimental recombinant snakebite antivenom based on an oligoclonal mixture of human monoclonal antibodies. *Biotechnology Journal*, *19*(10), Article e202400348. https://doi.org/10.1002/biot.202400348

Afroz, A., Siddiquea, B. N., Chowdhury, H. A., Jackson, T. N., & Watt, A. D. (2024). Snakebite envenoming: A systematic review and meta-analysis of global morbidity and mortality. *PLoS Neglected Tropical Diseases*, *18*(4), Article e0012080. https://doi.org/10.1371/journal.pntd.0012080

Afroz, A., Siddiquea, B. N., Shetty, A. N., Jackson, T. N., & Watt, A. D. (2023). Assessing knowledge and awareness regarding snakebite and management of snakebite envenoming in healthcare workers and the general population: A systematic review and meta-analysis. *PLOS Neglected Tropical Diseases*, *17*(2), Article e0011048. https://doi.org/10.1371/journal.pntd.0011048

Alangode, A., Rajan, K., & Nair, B. G. (2020). Snake antivenom: Challenges and alternate approaches. *Biochemical Pharmacology*, *181*, Article 114135. https://doi.org/10.1016/j.bcp.2020.114135

Albulescu, L. O., Xie, C., Ainsworth, S., Alsolaiss, J., Crittenden, E., Dawson, C. A., ... & Casewell, N. R. (2020). A therapeutic combination of two small molecule toxin inhibitors provides broad preclinical efficacy

against viper snakebite. *Nature Communications*, *11*(1), Article 6094. https://doi.org/10.1038/s41467-020-19981-6

Albuquerque, P. L. M. M., Da Silva Jr, G., Meneses, G. C., Martins, A. M. C., Raubenheimer, J., Shihana, F., ... & Daher, E. F. (2019a). SAT-158 renal tubular dysfunction, coagulation disturbances and novel biomarkers in acute kidney injury due to snakebites. *Kidney International Reports*, *4*(7), Article S71. https://doi.org/10.1016/j.ekir.2019.05.190

Albuquerque, P. L. M. M., da Silva Junior, G. B., Meneses, G. C., Martins, A. M. C., Lima, D. B., Raubenheimer, J., ... & Daher, E. D. F. (2019b). Acute kidney injury induced by Bothrops venom: Insights into the pathogenic mechanisms. *Toxins*, *11*(3), Article 148. https://doi.org/10.3390/toxins11030148

Alirahimi, E., Kazemi-Lomedasht, F., Shahbazzadeh, D., Habibi-Anbouhi, M., Chafi, M. H., Sotoudeh, N., ... & Behdani, M. (2018). Nanobodies as novel therapeutic agents in envenomation. *Biochimica et Biophysica Acta (BBA)-General Subjects*, *1862*(12), 2955-2965. https://doi.org/10.1016/j.bbagen.2018.08.019

Alirol, E., Sharma, S. K., Ghimire, A., Poncet, A., Combescure, C., Thapa, C., ... & Chappuis, F. (2017). Dose of antivenom for the treatment of snakebite with neurotoxic envenoming: Evidence from a randomised controlled trial in Nepal. *PLoS Neglected Tropical Diseases*, *11*(5), Article e0005612. https://doi.org/10.1371/journal.pntd.0005612

Alvitigala, B. Y., Gooneratne, L. V., Gnanathasan, C. A., & Wijewickrama, E. S. (2025). Snakebite-associated acute kidney injury in South Asia: Narrative review on epidemiology, pathogenesis and management. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *119*(6), 648-664. https://doi.org/10.1093/trstmh/trae077

Aphrodita, A., Sentono, D. N., Yudha, D. S., Purwestri, Y. A., Nuringtyas, T. R., Raharjo, S., ... & Sofyantoro, F. (2025). Comparative analysis of hemotoxic, myotoxic, and inflammatory profiles of Calloselasma rhodostoma and Trimeresurus insularis venoms in mice. *Narra J*, *5*(2), e1874-e1874. https://doi.org/10.52225/narraj.v5i2.1874

Arbel, Y., Ben-Assa, E., Puzhevsky, D., Litmanowicz, B., Galli, N., Chorin, E., ... & Finkelstein, A. (2019). Forced diuresis with matched hydration during transcatheter aortic valve implantation for reducing acute kidney injury: A randomized, sham-controlled study (REDUCE-AKI). *European Heart Journal*, *40*(38), 3169-3178. https://doi.org/10.1093/eurheartj/ehz343

Avau, B., Borra, V., Vandekerckhove, P., & De Buck, E. (2016). The treatment of snake bites in a first aid setting: A systematic review. *PLoS Neglected Tropical Diseases*, *10*(10), Article e0005079. https://doi.org/10.1371/journal.pntd.0005079

Azevedo-Marques, M. M., Cupo, P., Coimbra, T. M., Hering, S. E., Rossi, M. A., & Laure, C. J. (1985). Myonecrosis, myoglobinuria and acute renal failure induced by South American rattlesnake (*Crotalus durissus terrificus*) envenomation in Brazil. *Toxicon*, *23*(4), 631-636. https://doi.org/10.1016/0041-0101(85)90367-8

Barnes, K., Ngari, C., Parkurito, S., Wood, L., Otundo, D., Harrison, R., ... & Baker, C. (2021). Delays, fears and training needs: Perspectives of health workers on clinical management of snakebite revealed by a qualitative study in Kitui County, Kenya. *Toxicon: X*, *11*, Article 100078. https://doi.org/10.1016/j.toxcx.2021.100078

Bhuvaneshwari, B., & Umarani, U. (2022). A study of incidence of acute kidney injury in snake bite. *Global Journal for Research Analysis*, *11*(12), 34–37. https://doi.org/10.36106/gjra/1307569

Bickler, P. E. (2020). Amplification of snake venom toxicity by endogenous signaling pathways. *Toxins*, *12*(2), Article 68. https://doi.org/10.3390/toxins12020068

Boer-Lima, P. A., & Cruz-HÃ, M. A. (2002). Bothrops moojeni snake venom-induced renal glomeruli changes in rat. *The American Journal of Tropical Medicine and Hygiene*, *67*(2), 217-222. https://doi.org/10.4269/ajtmh.2002.67.217

Bonilla-Aldana, D. K., Bonilla-Aldana, J. L., Ulloque-Badaracco, J. R., Al-kassab-Córdova, A., Hernandez-Bustamante, E. A., Alarcon-Braga, E. A., ... & Suarez, J. A. (2024). Snakebite-associated infections: A systematic review and meta-analysis. *The American Journal of Tropical Medicine and Hygiene*, *110*(5), Article 874. https://doi.org/10.4269/ajtmh.23-0278

Braga, J. R. M., Jorge, A. R. C., Marinho, A. D., de Moraes Silveira, J. A., Nogueira-Junior, F. A., Valle, M. B., ... & Jorge, R. J. B. (2020). Renal effects of venoms of Mexican coral snakes Micrurus browni and Micrurus laticollaris. *Toxicon*, *181*, 45-52. https://doi.org/10.1016/j.toxicon.2020.04.095

Bush, S. P. (2004). Snakebite suction devices don't remove venom: They just suck. *Annals of Emergency Medicine*, *43*(2), 187-188. https://doi.org/10.1016/j.annemergmed.2003.10.031

Bustillo, S., García-Denegri, M. E., Gay, C., Van de Velde, A. C., Acosta, O., Angulo, Y., ... & Leiva, L. (2015). Phospholipase A2 enhances the endothelial cell detachment effect of a snake venom metalloproteinase in the absence of catalysis. *Chemico-biological Interactions*, *240*, 30-36. https://doi.org/10.1016/j.cbi.2015.08.002

Cai, Q., Jing, R., Zhang, W., Tang, Y., Li, X., & Liu, T. (2020). Hydration strategies for preventing contrast-induced acute kidney injury: A systematic review and bayesian network meta-analysis. *Journal of Interventional Cardiology*, *2020*(1), Article 7292675. https://doi.org/10.1155/2020/7292675

Cavalcante, T. T. A., de Souza, M. B. S., Neves, J. C. F., Ibiapina, H. N. S., Barbosa, F. B. A., Bentes, K. O., ... & Sartim, M. A. (2023). Inflammatory profile associated with secondary infection from bothrops atrox snakebites in the Brazilian amazon. *Toxins*, *15*(9), Article 524. https://doi.org/10.3390/toxins15090524

Chaaithanya, I. K., Abnave, D., Bawaskar, H., Pachalkar, U., Tarukar, S., Salvi, N., ... & Gajbhiye, R. K. (2021). Perceptions, awareness on snakebite envenoming among the tribal community and health care providers of Dahanu block, Palghar District in Maharashtra, India. *Plos One*, *16*(8), Article e0255657. https://doi.org/10.1371/journal.pone.0255657

Chaisakul, J., Alsolaiss, J., Charoenpitakchai, M., Wiwatwarayos, K., Sookprasert, N., Harrison, R. A., ... & Casewell, N. R. (2019). Evaluation of the geographical utility of Eastern Russell's viper (Daboia siamensis) antivenom from Thailand and an assessment of its protective effects against venom-induced nephrotoxicity. *PLoS Neglected Tropical Diseases*, *13*(10), Article e0007338. https://doi.org/10.1371/journal.pntd.0007338

Chaisakul, J., Khow, O., Wiwatwarayos, K., Rusmili, M. R. A., Prasert, W., Othman, I., ... & Chaiyabutr, N. (2021). A biochemical and pharmacological characterization of phospholipase A2 and metalloproteinase fractions from Eastern Russell's viper (*Daboia siamensis)* venom: Two major components associated with acute kidney injury. *Toxins*, *13*(8), Article 521. https://doi.org/10.3390/toxins13080521

Chaisakul, J., Rusmili, M. R. A., Alsolaiss, J., Albulescu, L. O., Harrison, R. A., Othman, I., & Casewell, N. R. (2020). In vitro immunological cross-reactivity of Thai polyvalent and monovalent antivenoms with Asian viper venoms. *Toxins*, *12*(12), Article 766. https://doi.org/10.3390/toxins12120766

Chaiyabutr, N., Chanhome, L., Vasaruchapong, T., Laoungbua, P., Khow, O., Rungsipipat, A., ... & Sitprija, V. (2022). Comparative compositional and functional venomic profiles among venom specimens from juvenile, subadult and adult Russell's viper (*Daboia siamensis*): Correlation with renal pathophysiology in experimental rabbits. *Journal of Venomous Animals and Toxins including Tropical Diseases*, *28*, Article 20210111. https://doi.org/10.1590/1678-9199-JVATITD-2021-0111

Chaves, F., Gutiérrez, J., & Brenes, F. (1992). Pathological and biochemical changes induced in mice after intramuscular injection of venom from newborn specimens of the snake Bothrops asper (Terciopelo). *Toxicon*, *30*(9), 1099-1109. https://doi.org/10.1016/0041-0101(92)90055-A

Chuang, P. C., Chang, K. W., Cheng, S. Y., Pan, H. Y., Huang, K. C., Huang, Y. T., & Li, C. J. (2021). Benefits of early in-hospital antivenom administration to patients with *Protobothrops mucrosquamatus* envenomation. *The American Journal of Tropical Medicine and Hygiene*, *104*(1), Article 323. https://doi.org/10.4269/ajtmh.20-0659

Chugh, K. S. (1989). Snake-bite-induced acute renal failure in India. *Kidney International*, *35*(3), 891-907. https://doi.org/10.1038/ki.1989.70

da Silva, T. B., Aly, J., Figueira, M., da Gama Araújo, C. M., de Sousa, I. K. F., Tonin, A. A., ... & dos Santos Sousa, R. (2021). Epidemiological aspects of snakebites in the state of Amazonas, Brazil, from 2007 to 2017.

Revista de Patologia Tropical/Journal of Tropical Pathology, *50*(4), 315-326. https://doi.org/10.5216/rpt.v50i4.67841

Dineshkumar, T., Dhanapriya, J., Murugananth, S., Surendar, D., Sakthirajan, R., Rajasekar, D., ... & Gopalakrishnan, N. (2018). Snake envenomation-induced acute interstitial nephritis. *Integrative Medicine in Nephrology and Andrology*, *5*(1), 14-17.

Engel, C. E. (1979). How can you decide what to teach?. *Medical Journal of Australia*, *1*(10), 438-440. https://doi.org/10.5694/j.1326-5377.1979.tb127021.x

Gajbhiye, R. K., Chaaithanya, I. K., Munshi, H., Prusty, R. K., Mahapatra, A., Palo, S. K., ... & Mahale, S. D. (2023). National snakebite project on capacity building of health system on prevention and management of snakebite envenoming including its complications in selected districts of Maharashtra and Odisha in India: A study protocol. *PLoS One*, *18*(2), Article e0281809. https://doi.org/10.1371/journal.pone.0281809

Gamulin, E., Mateljak Lukačević, S., Halassy, B., & Kurtović, T. (2023). Snake antivenoms-toward better understanding of the administration route. *Toxins*, *15*(6), Article 398. https://doi.org/10.3390/toxins15060398

Gois, P. H. F., Martines, M. S., Ferreira, D., Volpini, R., Canale, D., Malaque, C., ... & Seguro, A. C. (2017). Allopurinol attenuates acute kidney injury following Bothrops jararaca envenomation. *PLoS Neglected Tropical Diseases*, *11*(11), Article e0006024. https://doi.org/10.1371/journal.pntd.0006024

Gutiérrez, J. M., Burnouf, T., Harrison, R. A., Calvete, J. J., Kuch, U., Warrell, D. A., & Williams, D. J. (2014). A multicomponent strategy to improve the availability of antivenom for treating snakebite envenoming. *Bulletin of the World Health Organization*, *92*(7), 526-532. https://doi.org/10.2471/BLT.13.132431

Gutiérrez, J. M., Calvete, J. J., Habib, A. G., Harrison, R. A., Williams, D. J., & Warrell, D. A. (2017a). Snakebite envenoming. *Nature Reviews Disease Primers*, *3*(1), 1-21. https://doi.org/10.1038/nrdp.2017.63

Gutiérrez, J. M., Escalante, T., & Rucavado, A. (2009). Experimental pathophysiology of systemic alterations induced by Bothrops asper snake venom. *Toxicon*, *54*(7), 976-987. https://doi.org/10.1016/j.toxicon.2009.01.039

Gutiérrez, J. M., Solano, G., Pla, D., Herrera, M., Segura, Á., Vargas, M., ... & Calvete, J. J. (2017b). Preclinical evaluation of the efficacy of antivenoms for snakebite envenoming: State-of-the-art and challenges ahead. *Toxins*, *9*(5), Article 163. https://doi.org/10.3390/toxins9050163

Hamza, M., Knudsen, C., Gnanathasan, C. A., Monteiro, W., Lewin, M. R., Laustsen, A. H., & Habib, A. G. (2021). Clinical management of snakebite envenoming: Future perspectives. *Toxicon: X*, *11*, Article 100079. https://doi.org/10.1016/j.toxcx.2021.100079

Herath, H. M. N. J., Wazil, A. W. M., Abeysekara, D. T. D. J., Jeewani, N. D. C., Weerakoon, K. G. A. D., Ratnatunga, N. V. I., ... & Kularatne, S. A. M. (2012). Chronic kidney disease in snake envenomed patients with acute kidney injury in Sri Lanka: A descriptive study. *Postgraduate Medical Journal*, *88*(1037), 138-142. https://doi.org/10.1136/postgradmedj-2011-130225

Horo, S. M., Mardi, V., Shankar Munda, S., & Minz, G. (2022). Study of clinical profile of acute renal failure in snake bite patients. *Global Journal for Research Analysis*, *11*(2), 26–27. https://doi.org/10.36106/gjra/6200978

Houcke, S., Pujo, J. M., Vauquelin, S., Lontsi Ngoula, G. R., Matheus, S., Nkontcho, F., ... & Kallel, H. (2023). Effect of the time to antivenom administration on recovery from snakebite envenoming-related coagulopathy in French Guiana. *PLoS Neglected Tropical Diseases*, *17*(4), Article e0011242. https://doi.org/10.1371/journal.pntd.0011242

Iliyasu, G., Tiamiyu, A. B., Daiyab, F. M., Tambuwal, S. H., Habib, Z. G., & Habib, A. G. (2015). Effect of distance and delay in access to care on outcome of snakebite in rural north-eastern Nigeria. *Rural and Remote Health*, *15*(4), 76-81. https://doi.org/10.22605/RRH3496

Isbister, G. K. (2010). Snakebite doesn't cause disseminated intravascular coagulation: coagulopathy and thrombotic microangiopathy in snake envenoming. In *Seminars in Thrombosis and Hemostasis*, 36(4), 444-451. https://doi.org/10.1055/s-0030-1254053

Isbister, G. K. (2023). Antivenom availability, delays and use in Australia. *Toxicon: X*, *17*, Article 100145. https://doi.org/10.1016/j.toxcx.2022.100145

Isbister, G. K. (2024). The critical time period for administering antivenom: Golden hours and missed opportunities. *Clinical Toxicology*, *62*(5), 277-279. https://doi.org/10.1080/15563650.2024.2352026

Isbister, G. K., Brown, S. G., Page, C. B., McCoubrie, D. L., Greene, S. L., & Buckley, N. A. (2013). Snakebite in Australia: A practical approach to diagnosis and treatment. *Medical Journal of Australia*, *199*(11), 763-768. https://doi.org/10.5694/mja12.11172

Islam, K., Seth, S., Roy, A., & Datta, A. K. (2020). Predictors of renal complications in children with hematotoxic snakebite. *Indian Pediatrics*, *57*(5), 427-430. https://doi.org/10.1007/s13312-020-1817-7

Kanjanabuch, T., & Sitprija, V. (2008, July). Snakebite nephrotoxicity in Asia. In *Seminars in Nephrology*, 28(4), 363-372. https://doi.org/10.1016/j.semnephrol.2008.04.005

Kasturiratne, A., Wickremasinghe, A. R., De Silva, N., Gunawardena, N. K., Pathmeswaran, A., Premaratna, R., ... & De Silva, H. J. (2008). The global burden of snakebite: A literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Medicine*, *5*(11), Article e218. https://doi.org/10.1371/journal.pmed.0050218

Khalek, I. S., Senji Laxme, R. R., Nguyen, Y. T. K., Khochare, S., Patel, R. N., Woehl, J., ... & Jardine, J. G. (2024). Synthetic development of a broadly neutralizing antibody against snake venom long-chain α-neurotoxins. *Science Translational Medicine*, *16*(735), Article eadk1867. https://doi.org/10.1126/scitranslmed.adk1867

Khimmaktong, W., Nuanyaem, N., Lorthong, N., Hodgson, W. C., & Chaisakul, J. (2022). Histopathological changes in the liver, heart and kidneys following Malayan pit viper (*Calloselasma rhodostoma*) envenoming and the neutralising effects of hemato polyvalent snake antivenom. *Toxins*, *14*(9), Article 601. https://doi.org/10.3390/toxins14090601

Knudsen, C., & Laustsen, A. H. (2018). Recent advances in next generation snakebite antivenoms. *Tropical Medicine and Infectious Disease*, *3*(2), Article 42. https://doi.org/10.3390/tropicalmed3020042

Kumar, M., Arcot Thanjan, M., Gopalakrishnan, N., Jeyachandran, D., Thanigachalam, D., & Ramanathan, S. (2022). Snake envenomation-induced acute kidney injury: Prognosis and long-term renal outcomes. *Postgraduate Medical Journal*, *98*(1158), 264-268. https://doi.org/10.1136/postgradmedj-2020-139021

Kusuma, W. A., Fadli, A., Fatriani, R., Sofyantoro, F., Yudha, D. S., Lischer, K., ... & Swasono, R. T. (2023). Prediction of the interaction between Calloselasma rhodostoma venom-derived peptides and cancer-associated hub proteins: A computational study. *Heliyon*, *9*(11), Article e21149. https://doi.org/10.1016/j.heliyon.2023.e21149

Laustsen, A. H., Gless, B. H., Jenkins, T. P., Meyhoff-Madsen, M., Bjärtun, J., Munk, A. S., ... & Lohse, B. (2022). In vivo neutralization of myotoxin II, a phospholipase A2 homologue from Bothrops asper venom, using peptides discovered via phage display technology. *ACS Omega*, *7*(18), 15561-15569. https://doi.org/10.1021/acsomega.2c00280

Ledsgaard, L., Laustsen, A. H., Pus, U., Wade, J., Villar, P., Boddum, K., ... & Karatt-Vellatt, A. (2022). In vitro discovery of a human monoclonal antibody that neutralizes lethality of cobra snake venom. *Mabs*, *14*(1), Article 2085536. https://doi.org/10.1080/19420862.2022.2085536

Ledsgaard, L., Wade, J., Jenkins, T. P., Boddum, K., Oganesyan, I., Harrison, J. A., ... & Karatt-Vellatt, A. (2023). Discovery and optimization of a broadly-neutralizing human monoclonal antibody against long-chain α-neurotoxins from snakes. *Nature Communications*, *14*(1), Article 682. https://doi.org/10.1038/s41467-023-36393-4

Lentz, T. L., Hawrot, E., & Wilson, P. T. (1987). Synthetic peptides corresponding to sequences of snake venom neurotoxins and rabies virus glycoprotein bind to the nicotinic acetylcholine receptor. *Proteins: Structure, Function, and Bioinformatics*, *2*(4), 298-307. https://doi.org/10.1002/prot.340020406

Levey, A. S., & James, M. T. (2017). Acute Kidney Injury. *Annals of Internal Medicine*, *167*(9), Article ITC66. https://doi.org/10.7326/AITC201711070

Li, X., Liu, C., Mao, Z., Li, Q., & Zhou, F. (2021). Timing of renal replacement therapy initiation for acute kidney injury in critically ill patients: a systematic review of randomized clinical trials with meta-analysis and trial sequential analysis. *Critical Care*, *25*(1), Article 15. https://doi.org/10.1186/s13054-020-03451-y

Maciel Salazar, G. K., Saturnino Cristino, J., Vilhena Silva-Neto, A., Seabra Farias, A., Alcântara, J. A., Azevedo Machado, V., ... & Sachett, J. (2021). Snakebites in "Invisible Populations": A cross-sectional survey in riverine populations in the remote western Brazilian Amazon. *PLoS Neglected Tropical Diseases*, *15*(9), Article e0009758. https://doi.org/10.1371/journal.pntd.0009758

Mahmood, M. A., Halliday, D., Cumming, R., Thwin, K. T., Myitzu, M., White, J., ... & Peh, C. A. (2019). Inadequate knowledge about snakebite envenoming symptoms and application of harmful first aid methods in the community in high snakebite incidence areas of Myanmar. *PLoS Neglected Tropical Diseases*, *13*(2), Article e0007171. https://doi.org/10.1371/journal.pntd.0007171

Marinho, A. D., de Moraes Silveira, J. A., Chaves Filho, A. J. M., Jorge, A. R. C., Júnior, F. A. N., Pereira, V. B. M., ... & Monteiro, H. S. A. (2021). Bothrops pauloensis snake venom-derived Asp-49 and Lys-49 phospholipases A2 mediates acute kidney injury by oxidative stress and release of inflammatory cytokines. *Toxicon*, *190*, 31-38. https://doi.org/10.1016/j.toxicon.2020.12.004

Masci, P. P., Rowe, E. A., Whitaker, A. N., & De Jersey, J. (1990). Fibrinolysis as a feature of disseminated intravascular coagulation (DIC) after Pseudonaja textilis textilis envenomation. *Thrombosis Research*, *59*(5), 859-870. https://doi.org/10.1016/0049-3848(90)90399-W

Mejri, H., Mokrani, R., Ksouri, A., Seddik, M., Awad, N., Ayme, G., ... & Bouhaouala-Zahar, B. (2024). Neutralizing nanobodies against venoms from Naja haje species captured in north africa. *Toxins*, *16*(9), Article 393. https://doi.org/10.3390/toxins16090393

Menzies, S. K., Patel, R. N., & Ainsworth, S. (2025). Practical progress towards the development of recombinant antivenoms for snakebite envenoming. *Expert Opinion on Drug Discovery*, *20*(6), 799-819. https://doi.org/10.1080/17460441.2025.2495943

Michael, G. C., Thacher, T. D., & Shehu, M. I. (2011). The effect of pre-hospital care for venomous snake bite on outcome in Nigeria. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *105*(2), 95-101. https://doi.org/10.1016/j.trstmh.2010.09.005

Monteiro, W. M., Farias, A. S. D., Val, F., Neto, A. V. S., Sachett, A., Lacerda, M., ... & Wen, F. H. (2020). Providing antivenom treatment access to all Brazilian Amazon indigenous areas: 'Every life has equal value'. *Toxins*, *12*(12), Article 772. https://doi.org/10.3390/toxins12120772

Nduwayezu, R., Kinney, H., Amuguni, J. H., & Schurer, J. M. (2020). Snakebite envenomation in Rwanda: Patient demographics, medical care, and antivenom availability in the formal healthcare sector. *The American Journal of Tropical Medicine and Hygiene*, *104*(1), Article 316. https://doi.org/10.4269/ajtmh.20-0976

Nirja, K., & Rathore, S. S. (2020). Risk factor analysis for acute kidney injury in snake bite: Retrospective study from Western Rajasthan. *Scholars Journal of Applied Medical Sciences*, *08*(04), 1098–1101.

Noutsos, T., Currie, B. J., Isoardi, K. Z., Brown, S. G., & Isbister, G. K. (2022a). Snakebite-associated thrombotic microangiopathy: An Australian prospective cohort study [ASP30]. *Clinical Toxicology*, *60*(2), 205-213. https://doi.org/10.1080/15563650.2021.1948559

Noutsos, T., Currie, B. J., Lek, R. A., & Isbister, G. K. (2020). Snakebite associated thrombotic microangiopathy: A systematic review of clinical features, outcomes, and evidence for interventions including plasmapheresis. *PLoS Neglected Tropical Diseases*, *14*(12), Article e0008936. https://doi.org/10.1371/journal.pntd.0008936

Noutsos, T., Currie, B. J., Wijewickrama, E. S., & Isbister, G. K. (2022b). Snakebite associated thrombotic microangiopathy and recommendations for clinical practice. *Toxins*, *14*(1), Article 57. https://doi.org/10.3390/toxins14010057

Oukkache, N., Jaoudi, R. E., Ghalim, N., Chgoury, F., Bouhaouala, B., Mdaghri, N. E., & Sabatier, J. M. (2014). Evaluation of the lethal potency of scorpion and snake venoms and

comparison between intraperitoneal and intravenous injection routes. *Toxins*, *6*(6), 1873-1881. https://doi.org/10.3390/toxins6061873

Parihar, V., Mittal, A., Vikarn, V., Didel, S., & Singh, K. (2023). Venom-induced consumptive coagulopathy leading to thrombotic microangiopathy following Echis carinatus sochureki bite: Is snake antivenom effective?. *Journal of Tropical Pediatrics*, *69*(1), Article fmac113. https://doi.org/10.1093/tropej/fmac113

Parker-Cote, J., & Meggs, W. J. (2018). First aid and pre-hospital management of venomous snakebites. *Tropical Medicine and Infectious Disease*, *3*(2), Article 45. https://doi.org/10.3390/tropicalmed3020045

Patil, S., Paranjape, A., Patil, N. R., Patil, H. S., Surve, R. A., & Desai, M. B. (2019). Rural set up experience of viper bite treatment with special reference to FFP in venom induced consumption coagulopathy. *The Journal of the Association of Physicians of India*, *67*(10), 26-28.

Patra, A., & Mukherjee, A. K. (2021). Assessment of snakebite burdens, clinical features of envenomation, and strategies to improve snakebite management in Vietnam. *Acta Tropica*, *216*, Article 105833. https://doi.org/10.1016/j.actatropica.2021.105833

Pechprasarn, S., Wetchasit, P., & Pongsuwan, S. (2025). Optimizing chronic kidney disease prediction: A machine learning approach with minimal diagnostic predictors. *Journal of Current Science and Technology*, *15*(1), Article 76. https://doi.org/10.59796/jcst.V15N1.2025.76

Plackett, R., Kaushal, A., Kassianos, A. P., Cross, A., Lewins, D., Sheringham, J., ... & von Wagner, C. (2020). Use of social media to promote cancer screening and early diagnosis: Scoping review. *Journal of Medical Internet Research*, *22*(11), Article e21582. https://doi.org/10.2196/21582

Ponraj, D., & Gopalakrishnakone, P. (1995). Morphological changes induced by a generalized myotoxin (myoglobinuria-inducing toxin) from the venom of Pseudechis australis (king brown snake) in skeletal muscle and kidney of mice. *Toxicon*, *33*(11), 1453-1467. https://doi.org/10.1016/0041-0101(95)00091-Y

Priyamvada, P. S., Jaswanth, C., Zachariah, B., Haridasan, S., Parameswaran, S., & Swaminathan, R. P. (2020). Prognosis and long-term outcomes of acute kidney injury due to snake envenomation. *Clinical Kidney Journal*, *13*(4), 564-570. https://doi.org/10.1093/ckj/sfz055

Prowle, J. R., Chua, H. R., Bagshaw, S. M., & Bellomo, R. (2012). Clinical review: Volume of fluid resuscitation and the incidence of acute kidney injury-a systematic review. *Critical Care*, *16*(4), Article 230. https://doi.org/10.1186/cc11345

Prowle, J. R., Kirwan, C. J., & Bellomo, R. (2014). Fluid management for the prevention and attenuation of acute kidney injury. *Nature Reviews Nephrology*, *10*(1), 37-47. https://doi.org/10.1038/nrneph.2013.232

Pujo, J. M., Houcke, S., Ngoulla, G. R. L., Laurent, V., Signaté, B., Mutricy, R., ... & Kallel, H. (2025). Effectiveness of late and very late antivenom administration on recovery from snakebite-induced coagulopathy in French Guiana: A population-based study. *The Lancet Regional Health–Americas*, *42*. Article 100994. https://doi.org/10.1016/j.lana.2025.100994

Rao, P. S. K., Priyamvada, P. S., & Bammigatti, C. (2025). Snakebite envenomation-associated acute kidney injury: A South-Asian perspective. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *119*(7), Article trae114. https://doi.org/10.1093/trstmh/trae114

Ratanabanangkoon, K. (2023). Polyvalent snake antivenoms: Production strategy and their therapeutic benefits. *Toxins*, *15*(9), Article 517. https://doi.org/10.3390/toxins15090517

Rathnayaka, R. M. M. K., Ranathunga, P. E. A. N., & Kularatne, S. A. M. (2021). Thrombotic microangiopathy, hemolytic uremic syndrome and thrombotic thrombocytopenic purpura: Rare manifestations of Russell's viper (*Daboia russelii*) envenoming in Sri Lanka. *Asia Pacific Journal of Medical Toxicology*, *10*(3), 117-123. https://doi.org/10.22038/apjmt.2021.18818

Ratnayake, I., Mohamed, F., Buckley, N. A., Gawarammana, I. B., Dissanayake, D. M., Chathuranga, U., ... & Isbister, G. K. (2019). Early identification of acute kidney injury in Russell's viper (*Daboia russelii*) envenoming

using renal biomarkers. *PLoS Neglected Tropical Diseases*, *13*(7), Article e0007486. https://doi.org/10.1371/journal.pntd.0007486

Resiere, D., Mehdaoui, H., & Gutiérrez, J. M. (2018). Snakebite envenomation in the Caribbean: The role of medical and scientific cooperation. *PLoS Neglected Tropical Diseases*, *12*(7), Article e0006441. https://doi.org/10.1371/journal.pntd.0006441

Ryan, S. E., & Yong, J. L. (2002). Acute myotoxic and nephrotoxic effects of Aipysurus laevis venom following intramuscular injection in mice. *Experimental and Toxicologic Pathology*, *54*(1), 61-67. https://doi.org/10.1078/0940-2993-00232

Saladini, L. Y., Magalhães-Junior, M. J., da Silva, C. C. F., Oliveira, P. G. C., Kodama, R. T., Gomes, L., ... & Portaro, F. C. V. (2024). Evaluation of the inhibitory potential of synthetic peptides homologous to CDR3 regions of a monoclonal antibody against Bothropic venom serine proteases. *International Journal of Molecular Sciences*, *25*(10), Article 5181. https://doi.org/10.3390/ijms25105181

Salah Eldin, H., & Hafez, R. (2017). Clinical and laboratory parameters associated with acute kidney injury in viper envenomed cases. *Ain Shams Journal of Forensic Medicine and Clinical Toxicology*, *29*(2), 80-88. https://doi.org/10.21608/ajfm.2017.18212

Samuel, S. P., Chinnaraju, S., Williams, H. F., Pichamuthu, E., Subharao, M., Vaiyapuri, M., ... & Vaiyapuri, S. (2020). Venomous snakebites: Rapid action saves lives a multifaceted community education programme increases awareness about snakes and snakebites among the rural population of Tamil Nadu, India. *PLoS Neglected Tropical Diseases*, *14*(12), Article e0008911. https://doi.org/10.1371/journal.pntd.0008911

Sanhajariya, S., Duffull, S. B., & Isbister, G. K. (2018). Pharmacokinetics of snake venom. *Toxins*, *10*(2), Article 73. https://doi.org/10.3390/toxins10020073

Sarkar, S., Sinha, R., Chaudhury, A. R., Maduwage, K., Abeyagunawardena, A., Bose, N., ... & McCulloch, M. (2021). Snake bite associated with acute kidney injury. *Pediatric Nephrology*, *36*(12), 3829-3840. https://doi.org/10.1007/s00467-020-04911-x

Sartim, M. A., Cezarette, G. N., Jacob-Ferreira, A. L., Frantz, F. G., Faccioli, L. H., & Sampaio, S. V. (2017). Disseminated intravascular coagulation caused by moojenactivase, a procoagulant snake venom metalloprotease. *International Journal of Biological Macromolecules*, *103*, 1077-1086. https://doi.org/10.1016/j.ijbiomac.2017.05.146

Senthilkumaran, S., Patel, K., Salim, A., Vijayakumar, P., Williams, H. F., Vaiyapuri, R., ... & Vaiyapuri, S. (2021). Neutrophil gelatinase–associated lipocalin acts as a robust early diagnostic marker for renal replacement therapy in patients with Russell's viper bite–induced acute kidney injuries. *Toxins*, *13*(11), Article 797. https://doi.org/10.3390/toxins13110797

Shankar, T., Arora, P., Jose, J. R., & Kaushik, A. (2024). Thrombotic microangiopathy following a white-lipped pit viper envenomation. *BMJ Case Reports CP*, *17*(5), Article e258813. https://doi.org/10.1136/bcr-2023-258813

Sharma, N., Chauhan, S., Faruqi, S., Bhat, P., & Varma, S. (2005). Snake envenomation in a north Indian hospital. *Emergency Medicine Journal*, *22*(2), 118-120. https://doi.org/10.1136/emj.2003.008458

Silva, A., & Isbister, G. K. (2020). Current research into snake antivenoms, their mechanisms of action and applications. *Biochemical Society Transactions*, *48*(2), 537-546. https://doi.org/10.1042/BST20190739

Silva, A., Gunawardena, P., Weilgama, D., Maduwage, K., & Gawarammana, I. (2012). Comparative in-vivo toxicity of venoms from South Asian hump-nosed pit vipers (Viperidae: Crotalinae: Hypnale). *BMC Research Notes*, *5*(1), Article 471. https://doi.org/10.1186/1756-0500-5-471

Sofyantoro, F., Yudha, D. S., Lischer, K., Nuringtyas, T. R., Putri, W. A., Kusuma, W. A., ... & Swasono, R. T. (2022). Bibliometric analysis of literature in snake venom-related research worldwide (1933–2022). *Animals*, *12*(16), Article 2058. https://doi.org/10.3390/ani12162058

Suchonwanich, N., & Wananukul, W. (2018). Improving access to antidotes and antivenoms, Thailand. *Bulletin of the World Health Organization*, *96*(12), Article 853. https://doi.org/10.2471/BLT.18.217075

Tan, C. H., Leong, P. K., Fung, S. Y., Sim, S. M., Ponnudurai, G., Ariaratnam, C., ... & Tan, N. H. (2011). Cross neutralization of Hypnale hypnale (hump-nosed pit viper) venom by polyvalent and monovalent Malayan pit viper antivenoms in vitro and in a rodent model. *Acta Tropica*, *117*(2), 119-124. https://doi.org/10.1016/j.actatropica.2010.11.001

Tohamy, A. A., Mohamed, A. F., Moneim, A. E. A., & Diab, M. S. (2014). Biological effects of Naja haje crude venom on the hepatic and renal tissues of mice. *Journal of King Saud University-Science*, *26*(3), 205-212. https://doi.org/10.1016/j.jksus.2014.01.003

Uko, S. O., Malami, I., Ibrahim, K. G., Lawal, N., Bello, M. B., Abubakar, M. B., & Imam, M. U. (2024). Revolutionizing snakebite care with novel antivenoms: Breakthroughs and barriers. *Heliyon*, *10*(3). Article e25531. https://doi.org/10.1016/j.heliyon.2024.e25531

Vaara, S. T., Ostermann, M., Bitker, L., Schneider, A., Poli, E., Hoste, E., ... & Bellomo, R. (2021). Restrictive fluid management versus usual care in acute kidney injury (REVERSE-AKI): A pilot randomized controlled feasibility trial. *Intensive Care Medicine*, *47*(6), 665-673. https://doi.org/10.1007/s00134-021-06401-6

Van Oirschot, J., Ooms, G. I., Okemo, D. J., Waldmann, B., & Reed, T. (2021). An exploratory focus group study on experiences with snakebites: Health-seeking behaviour and challenges in rural communities of Kenya. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *115*(6), 613-618. https://doi.org/10.1093/trstmh/trab059

Variawa, S., Buitendag, J., Marais, R., Wood, D., & Oosthuizen, G. (2021). Prospective review of cytotoxic snakebite envenomation in a paediatric population. *Toxicon*, *190*, 73-78. https://doi.org/10.1016/j.toxicon.2020.12.009

Villalta, M., Sampaio, T. L., Lima, D. B., Jorge, A. R. C., Alves, R. S., Monteiro, H. S. A., ... & Gutiérrez, J. M. (2019). Nephrotoxicity induced by the venom of Hypnale hypnale from Sri Lanka: Studies on isolated perfused rat kidney and renal tubular cell lines. *Toxicon*, *165*, 40-46. https://doi.org/10.1016/j.toxicon.2019.04.014

Wade, J., Rimbault, C., Ali, H., Ledsgaard, L., Rivera-de-Torre, E., Abou Hachem, M., ... & Laustsen, A. H. (2022). Generation of multivalent nanobody-based proteins with improved neutralization of long α-neurotoxins from elapid snakes. *Bioconjugate Chemistry*, *33*(8), 1494-1504. https://doi.org/10.1021/acs.bioconjchem.2c00220

Waiddyanatha, S., Silva, A., Siribaddana, S., & Isbister, G. K. (2019). Long-term effects of snake envenoming. *Toxins*, *11*(4), Article 193. https://doi.org/10.3390/toxins11040193

Waiddyanatha, S., Silva, A., Weerakoon, K., Siribaddana, S., & Isbister, G. K. (2023). Does snake envenoming cause chronic kidney disease? A cohort study in rural Sri Lanka. *Clinical Toxicology*, *61*(1), 47-55. https://doi.org/10.1080/15563650.2022.2147843

Wijewickrama, E. S., Mohamed, F., Gawarammana, I. B., Endre, Z. H., Buckley, N. A., & Isbister, G. K. (2021). Serum and urinary biomarkers for early detection of acute kidney injury following *Hypnale* spp. envenoming. *PLoS Neglected Tropical Diseases*, *15*(12), Article e0010011. https://doi.org/10.1371/journal.pntd.0010011

Xie, C., Albulescu, L. O., Bittenbinder, M. A., Somsen, G. W., Vonk, F. J., Casewell, N. R., & Kool, J. (2020). Neutralizing effects of small molecule inhibitors and metal chelators on coagulopathic Viperinae snake venom toxins. *Biomedicines*, *8*(9), Article 297. https://doi.org/10.3390/biomedicines8090297

Zhang, L., Chen, Z., Diao, Y., Yang, Y., & Fu, P. (2015). Associations of fluid overload with mortality and kidney recovery in patients with acute kidney injury: A systematic review and meta-analysis. *Journal of Critical Care*, *30*(4), Article 860.e7-860.e13. https://doi.org/10.1016/j.jcrc.2015.03.025

Zhang, L., Kang, Y., Fu, P., Cao, Y., Shi, Y., Liu, F., ... & Qin, W. (2012). Myoglobin clearance by continuous venous-venous haemofiltration in rhabdomyolysis with acute kidney injury: A case series. *Injury*, *43*(5), 619-623. https://doi.org/10.1016/j.injury.2010.08.031

Zhu, H., Pan, Y., Tai, Z., Wang, M., Liu, X., Yu, X., & He, Q. (2025). Epitope-based antibody development against metalloproteinases and phospholipases A2 from Deinagkistrodon acutus venom. *Journal of Venomous Animals and Toxins Including Tropical Diseases*, *31*, Article e20240060. https://doi.org/10.1590/1678-9199-JVATITD-2024-0060