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NEPHROTOXICITY DUE TO SNAKE BITES

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ABSTRACT

Snakebites remain a critical public health issue in tropical countries, particularly due to their severe systemic effects, including nephrotoxicity and acute kidney injury (AKI). One major complication that frequently arises from envenomation, especially from Viperidae and Elapidae species, is AKI, which can progress to life-threatening conditions if not promptly managed. This study aims to explore the clinical management of snakebite-induced AKI and its systemic complications, using a case study of a 51-year-old male patient. The research employs a qualitative clinical case approach, involving observational analysis, serial laboratory tests, imaging, and documented treatment progression. The patient, who presented with swelling and bleeding in the bitten limb, was diagnosed with stage 3 AKI, Disseminated Intravascular Coagulation (DIC), and thrombocytopenia. Management included administration of antivenom, hemodialysis, and blood product transfusions. Significant improvements in kidney function and coagulation parameters were observed within two weeks. The findings highlight the urgency of early intervention, particularly in cases where the snake species is unidentified. This study contributes to a deeper understanding of AKI pathophysiology in envenomation and underscores the importance of WHO and KDIGO guideline implementation. It also emphasizes the need for enhanced clinical training and protocols in resource-limited settings to improve outcomes in snakebite victims.

KEYWORDS snakebite, acute kidney injury, nephrotoxic

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INTRODUCTION

Snakebites are a significant public health problem that causes considerable morbidity and mortality worldwide, particularly in the tropics. Kasturiratne *et al*. estimate that each year, there are at least 1.2 million snake bites, 421,000 cases of venomous snakes, and 20,000 deaths due to snake bites worldwide. Epidemiologically, it is said that men are bitten more often than women and can be affected at any age. Most snake bites occur in the population of farmers, plantation

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workers, herders, hunters, fishermen, fish farmers, restaurant snake workers, and snake handlers. Coagulopathy and neurotoxicity are the main clinical syndromes often arising from venomous snake bites. *Acute Kidney Injury* (AKI) is one of the complications that can occur as a result of a venomous snake bite, and there is growing evidence that AKI-related snakebites produce significant morbidity (Barrier et al., 2017a; Kanjanabuch & Sitprija, 2018a; Kasturiratne et al., 2018a; KDIGO, 2012a; Warrell, 2016a).

AKI is a life-threatening systemic effect that results from the bite of a venomous snake belonging to the families *Viperidae* and *Elapidae*. Three families of venomous snakes in Southeast Asia are the Elapidae, Viperidae, and Colubridae families. Some types of snakes that belong to the *Elapidae* family are Cobras (Naja), *kraits* (Bungarus), *death adders, taipans, black and brown snakes* (*Acanthophis, Oxyuranus, Pseudechis, Pseudonaja),* and sea snakes. These include the family *Viperidae*, namely *Russell's vipers (Daboia*), *saw-scaled vipers (Echis*), *Malayan pit vipers (Calloselasma), mamushi (Gloydius), hump-nosed pit-vipers (Hypnale), Chinese habu (Protobothrops mucrosquamatus), and green pit vipers (Trimeresurus*) and those belonging to the family *Colubridae*, namely the R*ed-necked keelback (Rhabdophis subminiatus)* and *Yamakagashi (R. tigrinus) (Gn et al., 2017; Gutiérrez et al., 2017; Kunti et al., 2021; Priyamvada et al., 2019; Tan et al., 2016).* The enzymatic poison in snake venom causes injury to all kidney cells, including glomeruli, tubulo-interstitials, and renal blood vessels. Pathogenesis of AKI due to secondary ischemia due to decreased renal blood flow caused by systemic bleeding and leakage of blood vessels, proteolytic degradation of the glomerular basement membrane by *snake venom metalloproteinases* (SVMPs), deposition of microthrombin in renal microvascular (thrombotic microangiopathy), direct cytotoxic action, systemic myotoxicity (rhabdomyolysis) and accumulation of large amounts of myoglobin in renal tubules (Goddard et al., 2011; Sarkar et al., 2021; Sitprija, 2016; Vikrant et al., 2017; Waikhom et al., 2012).

Clinical manifestations of AKI can be fatigue, loss of appetite, headache, nausea, vomiting, oliguria, and anuria. Monitoring of the development of AKI due to snake venom can be evaluated through blood pressure, fluid balance, serum creatinine, blood urea nitrogen, and serum electrolytes. Initiation of snake antivenom should be done immediately, regardless of fluid and electrolyte management. *Renal support, initiation, or emergency is indicated when* managing snakebites with AKI. Indications for *renal support* according to WHO 2016 include clinically obtained uremia, excess fluid resistant to diuresis, serum potassium > 7 mmol, symptomatic acidosis, increased creatinine >4mg/dl, and urea >130 mg/dl. Long-term monitoring is important because it is likely to be chronic kidney failure (Acharya & Naik, 2023; Metri, 2013; SK et al., 2022; Tchaou et al., 2020). In handling snake bites, it is necessary to manage quickly and ensure that the cause of the bite is caused by a venomous snake or not. Identification of the type of bite and symptoms caused by the bite is useful in the enforcement of diagnosis and therapy to avoid disability and life-threatening circumstances. In this case report, we will discuss a man bitten by a snake with AKI and bleeding manifestations.

Snakebites continue to pose a serious public health threat, especially in tropical regions such as Southeast Asia, where they result in thousands of cases of morbidity and mortality annually. Among the many systemic complications of

venomous snakebites, Acute Kidney Injury (AKI) stands out as one of the most severe. The nephrotoxic effects of snake venom—often from the Viperidae and Elapidae families—can rapidly lead to renal failure, particularly when accompanied by hemotoxic and myotoxic syndromes. However, many patients and healthcare providers lack awareness about the specific mechanisms and early signs of AKI following envenomation, which delays appropriate treatment and increases the risk of long-term renal damage.

Although antivenom therapy and renal support are the mainstays of treatment, complications such as Disseminated Intravascular Coagulation (DIC), thrombocytopenia, and severe bleeding often coexist, complicating the clinical management of these patients. Moreover, most victims do not witness or identify the snake species, leading to accurate diagnosis and targeted intervention challenges. This case report emphasizes the importance of early recognition, appropriate use of antivenoms, and timely renal support in reducing morbidity and improving prognosis in patients with snakebite-induced AKI.

Given the high incidence of snakebites and the risk of life-threatening complications like AKI, there is an urgent need to increase clinical awareness and research efforts focused on snakebite nephrotoxicity. The delay in recognizing AKI and associated conditions such as DIC often results in preventable fatalities or chronic kidney damage. In rural and agricultural communities, where access to specialized care is limited, evidence-based case reports are vital for guiding frontline healthcare providers in early diagnosis and treatment. This research is crucial for improving survival rates and minimizing long-term renal sequelae in snakebite victims.

Previous studies have documented the global burden of snakebites and the prevalence of AKI as a major complication. Research by Kasturiratne et al. estimated over 400,000 venomous snakebites annually, with AKI contributing significantly to morbidity. Other studies, such as those by Sitprija and Kanjanabuch, describe how hemotoxic and myotoxic venom can cause damage to renal structures through mechanisms like glomerular ischemia, tubular necrosis, and microangiopathy.

Furthermore, the KDIGO 2012 and WHO 2016 guidelines provide standardized criteria for diagnosing and managing AKI, which is particularly relevant in snakebite-induced cases. These guidelines emphasize early intervention with antivenom and renal replacement therapy in patients with oliguria, elevated serum creatinine, and systemic bleeding. However, real-world implementation remains inconsistent despite this guidance, especially in rural healthcare systems.

Recent studies also highlight the long-term outcomes of SAKI (Snakebite-Associated AKI), showing that up to one-third of survivors may develop chronic kidney disease (CKD), prehypertension, or hypertension. This underscores the need for long-term follow-up and identifying early predictors of poor renal outcomes following envenomation.

Despite a growing understanding of SAKI, few clinical studies or case reports provide comprehensive documentation of both the acute presentation and long-term management of AKI due to snakebite, especially in Indonesia. Most existing literature focuses on generalized treatment protocols or laboratory studies, without addressing the complexities encountered in real-life emergency settings, including unidentified snake species and coexisting complications like DIC. This

report addresses that gap by offering a detailed analysis of clinical progression, laboratory monitoring, treatment strategy, and recovery.

This case report presents a unique perspective by detailing a real-life case of a snakebite victim who developed stage 3 AKI, DIC, and thrombocytopenia and successfully recovered following comprehensive treatment, including antivenom, dialysis, and supportive care. The novelty lies in the sequential documentation of clinical and laboratory markers that reflect the progression of kidney injury and coagulopathy. Furthermore, it emphasizes the management of snakebite complications in a setting where the type of snake was unknown—an often overlooked but common scenario.

This study aims to describe the clinical manifestation, diagnosis, and management of AKI and systemic coagulopathy resulting from a venomous snakebite, and to illustrate the efficacy of a comprehensive treatment strategy involving antivenom administration, dialysis, and blood product transfusions. This report aims to provide healthcare professionals with practical insights into the multidisciplinary approach to managing complex envenomation cases.

The findings of this report contribute valuable clinical insights that can enhance the early recognition and management of snakebite-induced AKI and related complications. It is a reference for emergency and nephrology practitioners, especially in resource-limited settings where snakebites are common and immediate snake identification is often impossible. Additionally, the case supports the adoption of WHO and KDIGO guidelines in snakebite nephropathy and reinforces the importance of long-term monitoring to prevent progression to chronic kidney disease.

RESEARCH METHOD

This study adopts a clinical case study method focusing on the real-time medical handling of a 51-year-old male patient presenting with nephrotoxic and hemotoxic complications following a snakebite. The research centers on the patient's sequential clinical developments and therapeutic interventions, including diagnostic procedures, laboratory investigations, imaging results, and treatment outcomes. The qualitative design allows for in-depth analysis of the patient's symptoms, diagnostic challenges, and Acute Kidney Injury (AKI) progression, including the onset of Disseminated Intravascular Coagulation (DIC), thrombocytopenia, and systemic inflammatory responses.

Data collection involved detailed medical observation, physical examinations, and serial laboratory tests such as complete blood counts, blood chemistry panels, coagulation profiles, blood gas analyses, and urinalysis. Imaging, including abdominal ultrasound, further supported the diagnosis. The patient's response to treatment—administration of antivenom serum, hemodialysis sessions, and blood product transfusions—was monitored and recorded over two weeks. The analysis adhered to clinical practice guidelines set by WHO (2016) and KDIGO (2012) for managing AKI and snake envenomation.

This method enables a nuanced exploration of the pathophysiology and clinical management of snakebite-associated AKI (SAKI), especially in cases where the snake species is unidentified. The study illustrates the real-world complexity of managing SAKI by integrating lab results with treatment responses

and underscores the need for early intervention and comprehensive supportive care. The findings contribute to medical literature by offering insights into AKI progression, therapeutic decisions, and recovery trajectory in snakebite cases—a scenario underrepresented in regional clinical documentation.

RESULTS AND DISCUSSION

A man, 51 years old, came to the surgical emergency department (ER) with the main complaint of pain in his left hand after being bitten by a snake for approximately 20 minutes before entering the hospital. The patient was bitten by a snake 1 time on the left hand while cleaning the garden (field), but the patient did not see the type and color of the snake. At that time, the patient was shocked by the pain in his left hand. Pain complaints are accompanied by swelling and bleeding in the left hand, which was bitten by a snake. The patient was then taken to Prof.Dr.I.G.N.G Ngoerah Hospital. Complaints of fever, shortness of breath, seizures, vomiting blood, bloody stools, and black bowel movements when entering the hospital were denied. No history of weight loss. There were no complaints, and it was said to be within normal limits. The patient said that 5 years ago he had a stone with a size said to be the size of a mung bean. A history of chronic diseases such as DM, hypertension, kidney disease, and heart disease is denied by the patient. The patient has had congenital abnormalities in the eye organs since childhood and has not been able to see since then. The patient has an allergy to paracetamol and a reaction, including itching all over the body. The patient worked as a rice farmer, his history of alcohol consumption, and smoking was denied.

Figure 1. Patient Photos

On physical examination, it was found that the general state of severity, consciousness GCS E4V5M6, blood pressure 148/80 mmHg, pulse rate 92 times per minute, sufficient content, strong, breathing 18 times per minute, axillary temperature 370 Celsius, VAS score: 4/10, oxygen saturation 98% of the water room. On eye examination: the conjunctiva does not appear anemic, the sclera does not show jaundice, the reflex pupil is normal, and there is no subconjunctival bleeding. ENT examination: Tonsils are not enlarged, the pharynx is normal, the tongue is normal, and the lips are normal. On examination of the neck, JVP was 5

cm + 2 cm H20, and no enlargement of the glands or stiffness of the spleen was found. On thoracic examination, the inspection appears symmetrical right and left at static and dynamic moments, cardiac auscultation: there is a single heart sound 1 and a single heart sound 2, regular, and no murmur. On lung examination: inspection shows symmetrical chest wall at static and dynamic moments, palpation: normal palpable focal phremitus in the right and left chest, percussion sonor of the right and left chest, on auscultation there is a sound of vesicular main breathing in the lower right lung, no rumbling and whezzing in the entire field of the right and left lungs. On abdominal examination, when the inspection does not appear to be distended, on auscultation, the intestinal noise sounds normal, on palpation, there is no pressure pain, and the liver and spleen are not palpable. On percussion, tympani is on the entire abdominal wall, and the liver spans 10 cm. In the region of superior ecstremity sinistra, 1 snakebite wound was found in the antebrachii sinistra region. On inspection, there was hyperemia, edema, and compressive pain accompanied by minimal bleeding in the bite wound of the antebrachii sinistra region.

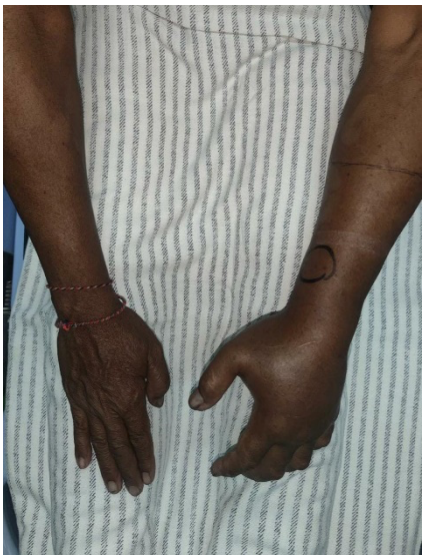

Figure 2. Bite wounds (9/5/22)

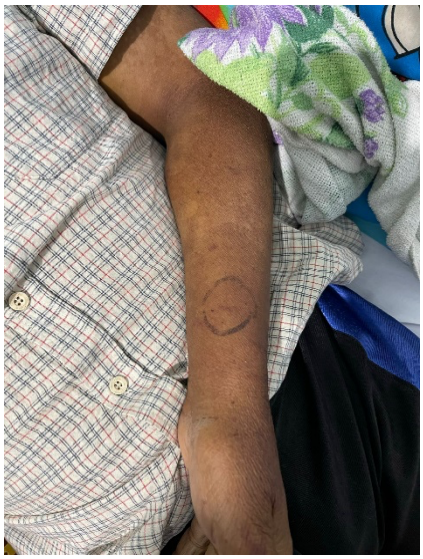

Figure 3. Bite wound (22/5/22)

In laboratory examinations upon admission to the hospital, complete blood tests, clinical chemistry, and blood gas analysis are periodically carried out, as described in the table below.

Table 1. Complete Blood Laboratory

DL	9/5	13/5	15/5	16/5	17/5	18/5	21/5	Unit	Normal values
WBC	10.07	14.47	15.81	14.48	16.04	12.36	14.43	103/µL	4.1 - 11.0
NE#	8.27	12.73	11.96	10.16	11.0	8.66	11.25	103/µLL	2.50 - 7.50
LY#	1.00	0.53	2.17	2.47	2.73	1.82	1.69	103/µL	1.00 - 4.00
HGB	12.40	10.90	9.10	8.50	8.70	8.50	11.0	g/dL	12-16
HCT	37.2	30.60	26.90	25.30	25.4	24.7	33.10	%	36-46
PLT	216	6	44	65	105	120	221	103/µL	140-440

Table 2. Blood Chemistry Laboratory

	9/5	11/5	12/5	13/5	14/5	15/5	16/5	17/5	Unit	Normal values
BUN	34.3	60.30	68.80	80.40	56.00	72.10	79.4	64.30	mg/dL	8.00-23.00
SC	4.07	5.85	5.05	5.43	3.77	4.09	4.09	3.68	mg/dL	0.72-1.25
GFR	35.88	10.25	12.25	11.22	17.44	15.8	15.8	17.96		>=90
APTT	30.7			>180	36.8	35.0	33.2	32.1	second	24-36
INR	0.87			19.15	2.06	1.73	1.44	1.17		0.9-1.1
PPT	10.0			>180	28.6	24.2	20.2	16.6	second	10.8-14.4
D-DIMER				4.31						
FIBRINOGEN				<30.0						

	18/5	19/5	20/5	21/5	22/5	23/5	24/5	Unit	Normal values
BUN	50.10	43.60	40.80	42.10	43.00	43.10	49.70	mg/dL	8.00-23.00
SC	3.42	3.46	3.40	3.30	3.13	3.35	3.31	mg/dL	0.72-1.25
GFR	19.62	19.34	19.76	20.48	21.84	20.12	20.41		>=90
APTT	33.9	22.3	32.3	31.5				second	24-36
INR	1.12	0.91	1.02	1.06					0.9-1.1
PPT	15.8	10.4	14.4	15.0				second	10.8-14.4
SODIUM			139		139	138	136	mmol/L	136-145
POTASSIUM			4.08		4.30	4.67	4.68	mmol/L	3.5-5.1

Table 3. Blood Gas Analysis Laboratory

AGDE	10/5	12/5	19/5	Unit	NormalValue
PH	7.27	7.27	7.45	-	7.35 - 7.45
PCO2	27	26	40	Mmhg	35.00 - 45.00
PO2	138	202	82	Mmhg	80.00- 100.00
BE	-14.5	-15	3.8	mmol/L	-2 - 2
HCO3	12.40	11.9	27.8	mmol/L	22.00 - 26.00
SO2	99	100	97	%	95-100
NA	126	112	133	mmol/L	136 - 145
K	4.10	4.20	3.70	mmol/L	3.50 - 5.10

Table 4. Urinalysis Laboratory

UL	11/5	24/5	Unit	Normal values
PH	5.0	5.5	-	4.5-8
Leukocyte	post++	pos++	leuco/ul	negative
Nitrite	negative	negative	mg/dl	negative
Protein	negative	(1+)	mg/dl	negative
Ketone	negative	negative	mg/dl	negative
Blood	(+2)	(+1)	ery/dl	negative

UL	11/5	24/5	Unit	Normal values
Glucose	negative	negative	mg/dl	negative
Urobilinogen	negative	negative	mg/dl	negative
Color	yellow	yellow		
Sediment leukocytes	18.9	17.1	/lpb	?2
Sedimentary erythrocytes	0.5	1.7	/lpb	?2

On May 11, 2022, the patient experienced an increase in serum creatinine by 5.85 mg/dL with a decrease in urine production of 200 cc for 24 hours (0.1 cc/kgbb/hour) and the patient underwent double lumen installation by a BTKV specialist colleague and was planned for cito hemodialysis with free heparin. During treatment, the patient underwent hemodialysis 3 times, namely on May 11, 13, and 17, 2022, using free heparin during hemodialysis. On May 13, 2022, the patient experienced bleeding gums and bleeding from the femoral double lumen access. At that time, leukocytosis of 14.47 x 10^3 /µL was obtained with a predominance of neutrophils (absolute 12.23 x 103 /µL) and thrombocytopenia of 6 x 103 /µL. Hemostasis failure was also increased, APTT > 180.0 seconds, INR 19.15, and PPT > 180.0, accompanied by an increase in D-Dimer of >4.31 and low Fibrinogen <30 mg/dl. Serum creatinine increased by 5.05 mg/dl, and the International Society of Thrombosis and Haemostasis (ISTH) score of 8, which means that it corresponds to the condition of Disseminated Intravascular Coagulation *(DIC).* The patient was examined for an abdominal ultrasound, and the results were obtained of bilateral chronic parenchymal kidney disease with a contracted left kidney, calcification of the prostate and the liver, gallbladder, spleen, pancreas, and bulging without abnormalities. The patient was diagnosed with Snakebite regio Antebrachii S with DIC hemotoxicity and thrombocytopenia. AKI

stage III ec renal ec snake bite with (improved) and asymptomatic hyponatremia, asymptomatic hypovolemic hypooosmolar ec susp SIADH.

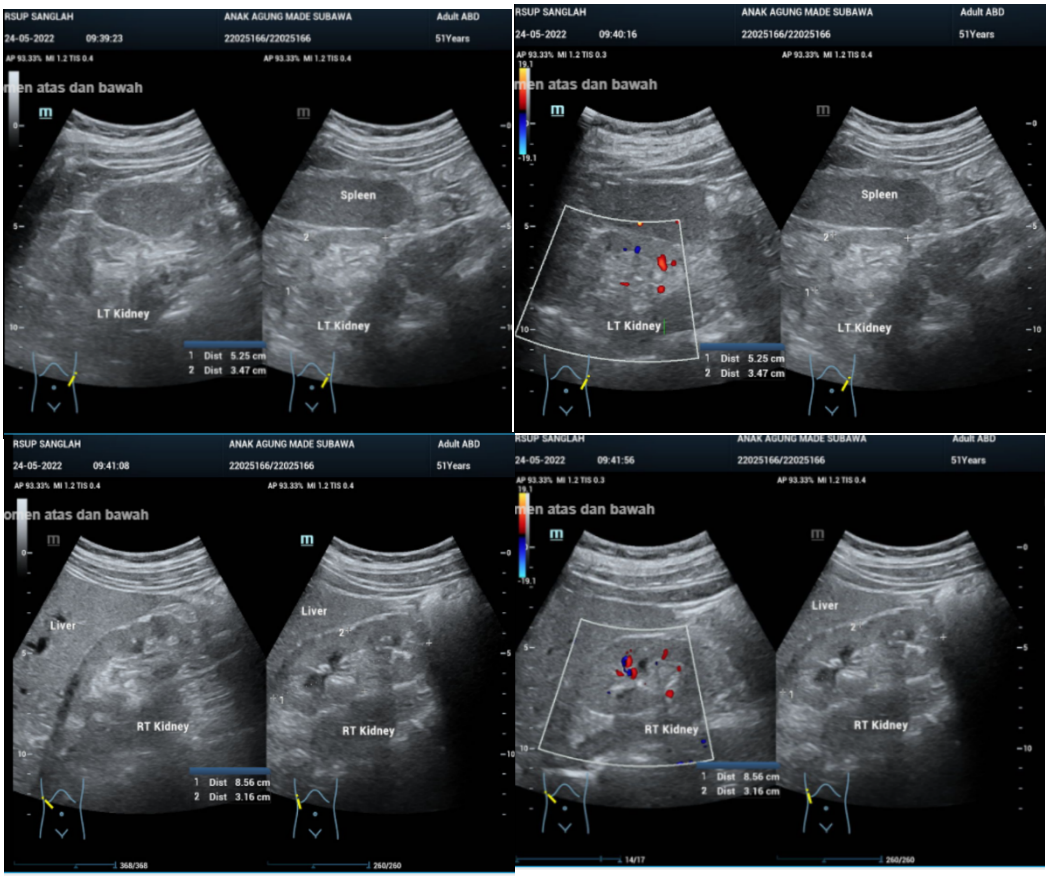

Figure 4. Upper Lower Abdominal Ultrasound

Patients were treated with NaCl 0.9% 1500cc/24 hours, FFP transfusion 5 intravenous bags, concentrated platelet transfusion 5 intravenous bags, omeprazole 40 mg every 12 hours intravenously, tranexamic acid 1 gram every 8 hours intravenously, dexamethasone 10 mg every 12 hours intravenously, diphenhydramine 10 mg every 8 hours IV Anti-Venom Serum (SABU) 2 ampoules in 500 ml D5% exhausted in 24 hours IV followed by SABU 2 ampoules in 500ml D5% exhausted in 8 hours IV, Anti Tetanus Serum and Tetanus Toxoid and pressure immobilization bandage by a fellow surgeon. Examination of hemostatic, renal, and kidney function is carried out every 24 hours and can be seen in Table 4.

On May 13, 2022, the patient was found to have bleeding gums, and the patient also experienced bleeding at the femoral double lumen access. On May 14, 2022, the patient received a 5-bag *thrombocyte concentrate* (TC) transfusion and a 5-bag *fresh frozen plasma* (FFP) transfusion. Due to the large amount of bleeding, the patient's Hb decreased to 8.5 g/dl, and it was planned to transfuse *packed red cells* (PRC) up to HB > 10g/dl. On May 18, 2022, bleeding and hemostasis improved, and urine production improved again at around 3000 cc/24 hours (1.8 cc/kg/hour).

Discussion

Snakebite cases are *a public health* phenomenon around the world that causes morbidity and mortality, especially in tropical areas. Southeast Asian snake bites usually occur in rice farmers, rubber plantation workers, coffee planters, fishermen, snake keepers, or when taking snake toxins. However, most bite victims do not know the type of snake that bites, which causes difficulties in identifying and determining the treatment choice. In India, it was reported that snake bites in 2005 caused about 23% of deaths in hospitals, and 13-32% of snakebites resulted in AKI, which Russell's Viper mainly caused. More than 3000 species of snakes are known worldwide, and about 600 species are venomous. The definitive diagnosis of a venomous snake bite is established based on the identification of the biting snake and the presence of clinical manifestations of the biting snake should be carried in a state of life or death, either part or all of the snake's body, but in conditions where there is no physical evidence of the snake, indirect identification of the patient's description, the form of the bite wound, the photograph of the snake, and the clinical syndrome of the symptoms and signs can be carried out. It is also necessary to distinguish whether the bite is from a non-venomous snake or another animal from a physical examination of the left bite wound. In this case, the patient was a farmer with a snakebite mark on the patient's left hand, but the patient did not see the snake biting him. Pain complaints are accompanied by swelling and bleeding in the left hand, which was bitten by a snake.

According to the WHO, the symptoms and clinical signs of snakebites can be divided into two, namely, local and systemic. Local symptoms and signs are swelling at the site of the snakebite, pain, local bleeding, *blistering, abscess, necrosis*, and signs of inflammation (warm red and swollen) while systemic symptoms that appear can be nausea, vomiting, malaise, limb weakness, hypotension, *faintness*, visual disturbances, ptosis, pulmonary edema, *spontaneous bleeding* (nosebleeds, bleeding gums, hematemesis*, cerebral hemorrhage*, melena, hematuria, *subconjunctive bleeding*) and AKI. In this case, there are signs of bite marks, pain, swelling, and bleeding in the wound. Meanwhile, systemic symptoms and signs are nausea, anuria, and bleeding in the hemodialysis access canal.

The clinical pattern of snake toxins can be broadly classified into five groups: neurotoxic, cytotoxic and hemotoxic, nephrotoxic, and myotoxic. Snake venom contains more than 100 enzymes (hydrolases, hyaluronidases, oxidases), proteins, peptides, and inorganic cations such as sodium, potassium, calcium, magnesium, and iron. Among them is the fact that it contains phospholipase A2, which plays an important role in the effects of systemic toxicity. Phospholipase A2 can cause damage to mitochondria, red blood cells, leukocytes, platelets, peripheral nerve endings, skeletal muscles, coagulation, vascular endothelium, and neuromuscular junctions. In the case of patients experiencing AKI as a nephrotoxic manifestation and bleeding due to the consumptive condition of coagulopathy as a hemotoxic manifestation.

AKI is an important complication of snakebites and a leading cause of death. Snakebite-associated AKI (SAKI) is a type of AKI that is reported to occur in 8.0-43.0% of patients with snakebite, of whom 15.0-55.0% require renal support, with a mortality rate of 8.0-39.0%. Kidney disorders include hematuria, oliguria, and anuria, usually in snake bites of the *Viperidae* family. AKI generally occurs after a bite from a myotoxic or hemotoxic snake. These snakes are *Russell's viper, saw-scaled viper*, *hump-nosed pit viper, green pit viper*, and sea snake. Russell*'s viper,*

saw-scaled viper, hump-nosed pit viper, and green pit viper snake toxins are hemotoxic. Sea snakes and *Russell's viper* are myotoxic. The myotoxic effects of sea snakes due to the enzyme Phospholipase A2 result in the destruction of muscle cells and cause rhabdomyolysis, which is manifested by muscle pain, weakness, paralysis, myoglobinuria, and increased serum creatinine phosphokinase, which can cause AKI. In snake bites of the *Viperidae* family, AKI can be accompanied by intravascular hemolysis or coagulation with hemoglobinuria and hematuria.

The definition of AKI in the case of snake bites according to WHO 2016 is a sudden decrease in kidney function within 48 hours, oliguria or anuria (0.5cc/kgbb/hour for more than 6 hours), an increase in serum creatinine ≥ 0.3 mg/dL or ≥ 26μmol or an increase ≥ 1.5 times the reference value, which is known or considered to have occurred within one week accompanied by uremia syndrome as according to KDIGO 2012 the criteria for AKI is a rapid decrease in the rate of glomerular filtration (LFG) in hours to weeks generally reversible, followed by the failure of the kidneys to excrete residual nitrogen metabolism, with or without a disturbance of fluid and electrolyte balance. AKI according to KDGIO 2012 is defined when any of the following criteria are met: serum creatinine rises by ≥ 0.3 mg/dL or ≥ 26μmol/L within 48 hours or Serum creatinine increases ≥ 1.5 times the reference value, known or thought to have occurred within one week or Urine output <0.5ml/kg/hour for> 6 consecutive hours. In the case of the patient experiencing an increase in serum creatinine by 4mg/dl and experiencing anuria for more than 12 hours. In the case of the patient experiencing snakebite-associated AKI (SAKI), which is characterized by anuria and increased serum creatinine, the management involves renal support. A kidney biopsy is not performed.

The pathogenesis of SAKI includes various mechanisms, namely hemodynamic disorders resulting in ischemia in the kidneys, proteolytic degradation of the glomerular membrane due to SVM, thrombotic microangiopathy (TMA), and direct nephrotoxicity due to activation of complex immune complements and hypersensitivity to snake toxins. Nephropathy in snake bites is very complex, involving the direct effects of snake toxin on the kidneys and the inflammatory impact due to the release of various cytokines and endogenous mediators. The enzyme Phospholipase A2 and metalloproteases are important toxin components of snake toxins in causing AKI. Hemodynamic changes caused by vasoactive mediators, cytokines, and direct nephrotoxicity significantly cause nephropathy, hemorrhage, hypotension, DIC, intravascular hemolysis, and rhabdomyolysis, thereby increasing renal ischemia due to decreased *renal blood flow* (RBF), resulting in AKI. AKI that arises within a few hours after a bite without symptoms of hypotension, bleeding, intravascular hemolysis, or rhabdomyolysis can occur as a result of direct nephrotoxicity of snake toxin, resulting in mesangiolysis, glomerulonephritis, and vasculitis. Pathological changes in the kidneys include tubular necrosis, cortical necrosis, interstitial nephritis, glomerulonephritis, and vasculitis. Sanjay et al's research in 2017 found that intravascular hemolysis and rhabdomyolysis are the main causes of AKI due to snakebites. *Acute tubular necrosis* (ATN) and *acute interstitial nephritis* (AIN) are common findings in renal histology, while *renal cortical necrosis* (RCN) is fewer.

An incident of AKI can occur a few hours to 96 hours after a bite. The duration of an AKI after a snake bite generally ranges from 2 to 3 weeks. Tubular necrosis is an important pathological correlate of AKI. Prolonged AKI with oligo-

anuria after a snakebite indicates cortical necrosis or acute tubular necrosis associated with interstitial nephritis or extracapillary glomerulonephritis. Acute glomerulonephritis in snake bites causes mild kidney failure. Patients usually fully recover except in cortical necrosis. An etiological diagnosis is made by a kidney biopsy, which indicates if the AKI does not improve within 3 weeks.

Table 5. Snakes in Asia are hemotoxic and nephrotoxic in nature

Types of Snakes	Toxicity	Mechanism	Nephropatht
Russell's Viper (Daboia russellii)	Koagulopati Thrombocytopenia Hemolysis Occasional rhabdomyolysis	Activation of Factor V and X Phospholipase A2	Tubular necrosis Cortical necrosis Interstitial nephritis Glomerulonephritis Mesangiolysis Vasculitis
Saw-scaled viper (Echis carinatus)	Koagulopati Thrombocytopenia Hemolysis	Activation of prothrombin and factor X	Tubular necrosis Cortical necrosis Glomerulonephritis
Hump-nosed pit viper (Hypnale hypnale)	Koagulopati Thrombocytopenia Hemolysis	Procoagulant action Fibrinolysis	Tubular necrosis Cortical necrosis
Green pit viper (*Cryptelytrops, Trimeresurus, Protobothrops*)	Koagulopati Thrombocytopenia	Thrombin-like action Fibrinolysis	Mesangiolysis Glomerulonephritis
Sea snake (*Hydrophinae*)	Rhabdomyolysis	Phospholipase A2	Tubular necrosis

The hemotoxic effects caused by snake toxin are characterized by local and systemic bleeding, such as bleeding on the gums, newly healed wounds, snake bite sites, gastrointestinal tract bleeding, genito-urinary, hematemesis, and hemoptysis. Bleeding caused by snake toxin results from *venom-induced consumption coagulation* (VICC). Various terms have been used to refer to the consumptive condition of coagulopathy due to snake toxins, including DIC. VICC arises due to the activation of coagulation cascades by snake toxins such as *thrombin-like enzymes* (TLE), prothrombin, and factor X activators, factor V activators that produce consumptive coagulopathy that causes the consumption of clotting factors, resulting in deficiencies of several factors. VICC results in increased D-dimer, prolongation *of prothrombin time* (PT), *international normalised ratio* (INR), and *activated partial thromboplastin time* (aPTT), as well as low fibrinogen [9]

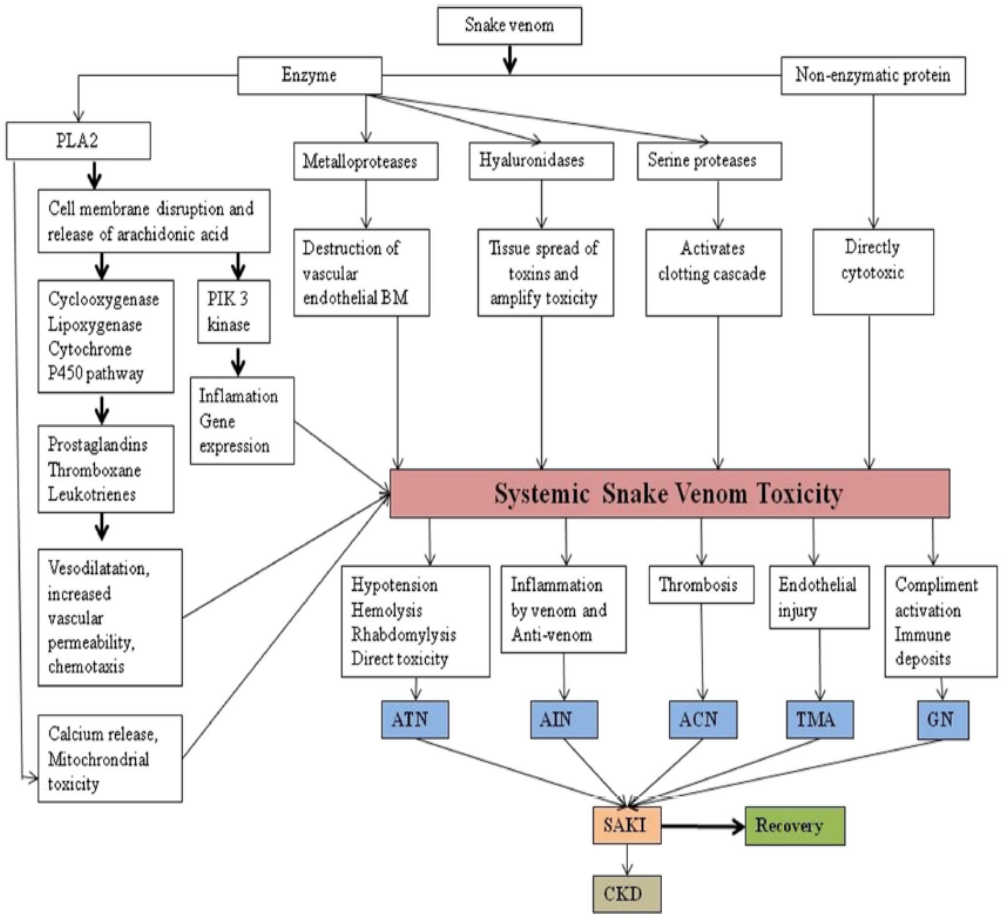

Figure 5. Pathogenesis of AKI due to snake toxin[7]

ATN Acute tubular necrosis, AIN = acute interstitial nephritis, TMA Thrombotic microangiopathy, GN Glomerulonephritis, ACN Acute renal cortical necrosis, SAKI = snakebite-associated acute Kidney Injury, CKD *Chronic Kidney Injury*.

The procedure in the case of a snakebite is that the patient must be taken to the hospital immediately, according to the WHO guidelines in 2016 first aid in the case of a snakebite is: efforts to calm the victim, immobilization of all limbs of the patient's body, especially the bitten limb ideally in a recovery position, speed up transportation to medical care, immobilization can be given *a simpler pressure-pad*, more practical than *pressure bandage* immobilize and never use tight tourniquets. Evidence of the type of snake biting is valuable evidence, but snakes do not have to be caught, killed, or handled (Barrier et al., 2017b; Kanjanabuch & Sitprija, 2018b; Kasturiratne et al., 2018b; KDIGO, 2012b; Warrel, 2016b). Close-up photos of snakes with mobile phones are very useful in enforcing diagnosis and selection of therapies. Traditional and popular first aid efforts in the community such as making local incisions in the area of the snakebite, sucking toxins from the bite wound, attaching tight tourniquets to the hands/feet affected by the snakebite, using certain herbs, and others are not recommended because they have the potential to endanger the victim or the rescuer. After being bitten by a snake, the patient was

immediately taken to the hospital at Prof. I.G.N.G Ngoerah Hospital and arrived within 20 minutes after being bitten. In the ER*, pressure immobilization bandages*, antivenoms, and anti-inflammatory administration were installed. The type of snake that bites is unknown because there is no physical evidence or photos of the snake biting.

Antivenom is the only specific antidote treatment against snake toxins. Snake antivenom serum is a fragment of immunoglobulin (Pepsin-refined $F(ab')_2$ purified from the plasma of horses or donkeys (*equine*) or sheep (*ovine*). Antivenom or antivenom serum can be monovalent (antibodies from 1 type of snake) or polyvalent (antibodies from various snakes). The use of monovalent antivenoms is more effective and has fewer side effects than polyvalent ones. However, the use of monovalent requires the exact identification of the type of snake that bites. In Indonesia, Biofarma produces polyvalent antivenoms that can overcome the neurotoxic toxins Naja sputatrix, Bungarus fasciatus, Daboia siamensis, Trimeresurus species, and all the Elapidae families. Administration of antivenom is recommended in patients who have been proven or suspected of having been bitten by a snake experiencing one or more of the following signs: hemostasis abnormalities (spontaneous systemic bleeding, coagulopathy or thrombocytopenia), neurotoxic signs (ptosis, external opthalmoplegia, paralysis, etc.), cardiovascular abnormalities (hypotension, shock, cardiac arrhythmia, abnormal ECG), AKI (oliguria/anuria, elevated serum creatinine/urea), haemoglobinuria/ myoglobinuria, and signs of local envenomation (local swelling of more than half of the bitten limb within 48 hours of the bite, rapid expansion of the swelling, and enlargement of lymph nodes). In cases where the type of snake that bites could not be identified, indications of antivenom administration were found, namely AKI, hemostasis abnormalities, and signs of local envenomation, so the patient was given antivenom serum for snake venom. In these patients, antivenom was administered at 2 vials in 500 cc NaCl 0.9% every 8 hours for 4 days.

In the case of patients with AKI and dialysis, the kidney function improved after undergoing Hemodialysis 3 times. Based on the KDIGO criteria, the patient experienced stage 3 AKI because of a 3-fold increase in serum creatinine from baseline and anuria for >12 hours. Dialysis is indicated in clinical uremia, fluid overload, oligouria or anuria > 12 hours, *electrolyte imbalance* (hyperkalemia K > 7mg/DL with or without ECG changes), intoxication, and metabolic acidosis. According to WHO 2016, dialysis indications in snakebites are in clinical uremia, fluid overload, blood biochemistry laboratory results obtained one or more, as creatinine > 4 mg/dl (500 µmol/L), urea >130 mg/dl (27 mmol/L), potassium >7 mmol/L (or change in ECG), and symptomatic acidosis. Waikhom et al, One-third of patients with AKI experienced long-term complications such as CKD, prehypertension, and hypertension at follow-up.

In the case of the patient experiencing bleeding at access to hemodialysis and experiencing hemostasis failure disorders. In snake bites that have hemotoccytes with clinical bleeding, platelet transfusions are recommended in patients with active bleeding with platelet counts <50,000/µl or those at high risk of bleeding with platelet counts <20,000/µl. Transfusions can be stopped when there is an increase in platelet count and fibrinogen levels. In the case of the patient

given a 5-sac TC transfusion, the clinical bleeding and laboratory results of the coagulation fail to improve.

CONCLUSION

A case involving a 51-year-old male patient who suffered a venomous snakebite highlights the severe complications that can arise, particularly hemotoxic effects such as Disseminated Intravascular Coagulation (DIC) and nephrotoxic effects resulting in Acute Kidney Injury (AKI). Immediate hospital referral is essential in such cases, and pre-hospital interventions should be avoided to prevent worsening the condition. The application of a pressure immobilization bandage is recommended to limit venom spread. The administration of antivenom remains the only specific treatment for neutralizing snake venom and should be considered when the clinical benefits outweigh the potential risks. Ideally, monovalent antivenom is preferred due to its lower risk of adverse reactions compared to polyvalent types. For patients experiencing active bleeding, platelet transfusions may be necessary. Hemodialysis should be initiated promptly if there are clear indications of kidney dysfunction or failure.

Suggestions for future research include conducting broader clinical studies on snakebite-induced AKI to identify predictive biomarkers for early renal involvement. Comparative studies on the efficacy and safety of monovalent versus polyvalent antivenoms could also help optimize treatment protocols. Furthermore, long-term follow-up studies on patients recovering from SAKI are needed to understand the risk of chronic kidney disease and inform preventive strategies in endemic areas.

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