

THE EFFECT OF SNAKEBITE ON HEMODYNAMIC DISORDERS OF THE HEART IN ADULTS AND PREGNANT WOMEN

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ABSTRACT

A snake bite is a natural defense response from a snake and can be an emergency medical situation. Snakes have a venom consisting of various proteins that can affect the functioning of the human body. The venom structure in snake venom varies between different species of snakes. Knowing the effect of snakebite on hemodynamic disorders of the heart in adults and pregnant women. This study is a Systematic Review that applies the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) method, which is a systematic approach that follows appropriate research steps and protocols. The result of this study is the association of Snakebite with Hemodynamic Disorders of the Heart in Adult Patients and Pregnant Women" showing a major focus on heart disorders, infections, muscle and bone necrosis due to poisonous snake bites in developing countries, especially in children. Snake bites can cause immediate cardiovascular effects such as anaphylactic reactions, electrolyte disturbances, to cardiogenic shock and cardiac arrest in severe cases. Effective treatment for osteomyelitis and cardiogenic shock due to snakebites involves extensive surgical debridement and antibiotic therapy tailored to culture results. The duration of therapy varies based on the type of infection, with longer treatments for chronic infections. Adequate debridement is key to successful treatment, and a variety of surgical methods can be used, including open surgery, arthroscopy, or puncture/aspiration and flushing.

INTRODUCTION

Snakebite is a defense mechanism of snakes and can be a medical emergency (Ferdian et al., 2023). Snake venom contains a mixture of protein components that affect functional activity on the target's physiology (Frangieh et al., 2021). The structure of venom in snake venom has different variations of different snake species. Snakebite can be life-threatening if it has neurotoxic, cytotoxic and hemotoxic toxic effects (Babangida & Baraya, 2020); (Slagboom et al., 2017).

In 2009, the WHO included *snakebite* in its list of neglected tropical diseases and a global problem. It is estimated that among the 3,500,000 cases of *snakebite*, 1,100,000 cases of poisoning, and about 60,000 deaths from *snakebite* each year. *Snakebite* is a significant cause of morbidity and mortality worldwide, especially in South and Southeast Asia, sub-Saharan Africa, and Latin America. (Adiwinata et al., 2015).

In Indonesia, there are an estimated 120,000 cases of snake bites with an estimated death rate of 20 to 11,581 people in 2007. The estimate is based on many influencing factors, such as the number of *snakebite* cases that occur in rural areas, improper traditional medicine, and handling does not reach the hospital. (Adiwinata & Nelwan, 2015); (Decho & Gutierrez, 2017)

The process of spreading *snakebite* venom begins after the snake bite appears a condition of local swelling. Swelling is usually detected within 2-4 hours and can expand rapidly until it reaches its peak on the second or third day. *Blistering* appears within 2-12 hours, and tissue necrosis is visible within 1 day after the bite (Resiere, Resiere, et al., 2020). The impact of complications from *snakebite* includes hemodynamic disorders. which most often occurs in children. It is known that 85% of patients with osteomyelitis are under 17 years old. Chronic osteomyelitis is a major health problem due to its significantly high morbidity (Martin et al., 2016).

In addition to osteomyelitis, another complication in *snakebite* cases is *cardiogenic shock*. According to research in hospitals in America at Mayo Clinic Hospital in 2016-2018, in 1029 the highest shock cases were single shock cases cardiac shock 65% followed by mixed shock 14%, sepsis shock 12% and the rest other shock.

Some studies report that *snakebite* is associated with severe complications such as nephrotoxicity, kidney failure, cardiotoxicity, tissue necrosis, osteomyelitis, aspiration pneumony and resulting in shock that can result in death. Understanding of the relationship between *snakebite* to osteomyelitis, and *cardiogenic shock* is rarely known and discussed in the review literature so that the background for researchers to examine the correlation of these variables. The objectives of this study are

1. Knowing the relationship of *snakebite* with hemodynamic disorders of the heart
2. Knowing the relationship between *snakebite* in adults and pregnant women.
3. Knowing the management of hemodynamic disorders of the heart due to complications

of snakebite.

The results of this study can be used as a source of information and reference for objective correlation regarding the effect of snakebite with hemodynamic disorders of the heart. The results of this study can add new insights and references in the field of medical science for the management of hemodynamic disorders of the heart due to snakebite complications. Handling in cases of adult and child patients requires study and it is important to know medical services in providing medical services in Indonesia.

RESEARCH METHODS

This research is a *Systematic Review* using the *Preferred Reporting Items for Systematic Reviews and Meta-analyses* method or commonly called PRISMA, this method is carried out systematically by following the correct research stages or protocols. *Systematic review* is one method that uses review, review, structured evaluation, classification, and categorization of *evidence based* that has been produced previously. The steps in implementing *systematic review* are very planned and structured so that this method is very different from the method that is just for delivering literature studies. *The procedure* of this *systematic review* consists of several steps, namely 1) compiling *Background and Purpose*, 2) *Research Question*, 3) *Searching for the literature* 4) *Selection Criteria* 5) *Practical Screen* 6) *Quality Checklist and Procedures* 6) *Data Extraction Strategy*, 7) *Data Synthesis Strategy*

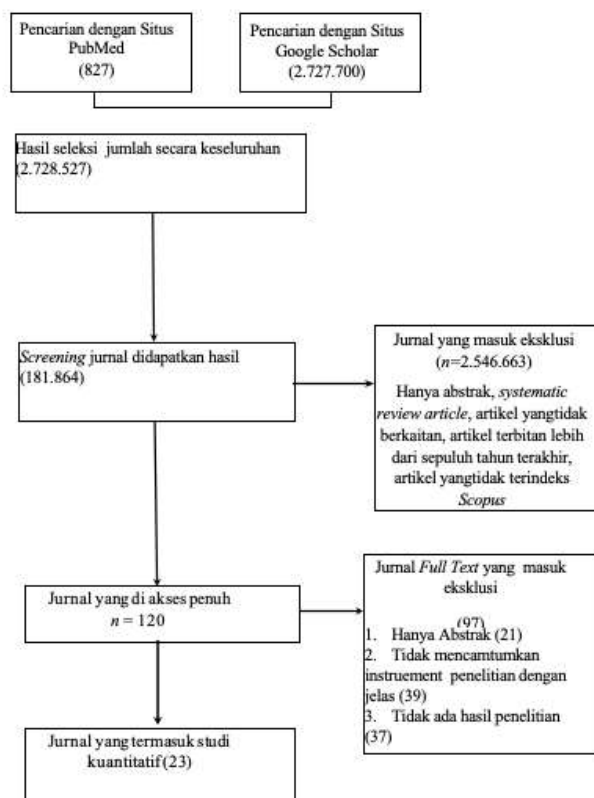


Figure 1. PRISMA diagram: Stages of systematic review

Research Data Base Source

The data used to search the literature is through the selection of literature based on the word *snakebite*, which concerns medical research. Next, apply a literature review related to *snakebite* with the incidence of *osteomyelitis*; *snakebite with the incidence of hemodynamic disorders of the heart* in adult patients and pregnant women. Articles are searched using PubMed and Google Scholar as databases. The search for research articles relevant to the research topic is done using the keyword; "*snakebite*". "*Osteomyelitis*", "*Haemodynamic Event*", "*Snakebite in adult patients and pregnant women*", "*Snakebite and osteomyelitis*" and "*Snakebite and hemodynamic disorders of the heart*".

Publication time

The journals taken are journals published in 2012-2022

Inclusion and exclusion criteria

1. Inclusion criteria

1. Research articles published in 2012-2022
2. The dependent variables in the research article were *osteomyelitis* and *cardiac shock* in pediatric and adult patients
3. The independent variable in the research article is *snakebite*
4. Articles indexed by Scopus 1, 2, 3 and 4
5. Exclusion criteria
6. Research articles with incomplete text
Artikel berbasis *literature review / systematic review*
7. Does not discuss dependent variables / unrelated articles
8. Articles with incomplete content

2. Publication Search Strategy

Searches for publications on Pubmed and Google Scholar use the selected keyword "*snakebite*". "*Osteomyelitis*", "*Haemodynamic Event*", "*Snakebite in adult patients and pregnant women*", "*Snakebite and osteomyelitis*" and "*Snakebite and Haemodynamic Event*".

RESULTS AND DISCUSSION

This chapter will describe the results and analysis using 181,864 journals related to the variable relationship of *snakebite* with the incidence of *osteomyelitis* and cardiac shock in pediatric and adult patients, with 120 journals that have been fully accessed. Journals obtained in screening are further sorted based on exclusion criteria, and extracted into a table to make it easier to explain the contents of the journal. Based on the results of journal clustering, it was found that the number of journals indexed by Scopus Q1 amounted to 6 journals, Q2 4 journals, Q3 amounted to 5 journals, and Q4 amounted to 8 journals, so that there were 23 journals extracted and used as a reference for *our systematic review* work.

Data Analysis

Data information about *snike bite* as an independent variable analyzed is presented in the form of a table containing journal title, year published, author, purpose, population / sample, research instrument, data analysis / research method, research results in journals and *Scopus index*.

Journal Analysis

No	Journal Title and Researcher Name (Year)	Result	Klasterization Journal
1	Snakebite envenoming in children: A neglected tropical disease in a Costa Rican pediatric tertiary care center Helena Brenes-Chacóna, José María Gutiérrez b, Kattia Camacho-Badillaa, Alejandra Soriano-Fallasa, Rolando Ulloa-Gutiérreza, Kathia	80 patients (PTS) admitted and classified as having mild (17 points, 29.3%), moderate (58 points, 72.5%) or severe (5 points, 6.2%) toxins. 52/80 (65%) patients received treatment within the first four hours, three (3.75%) between 5–8 hours, three between 9–12 noon, four (4%) between 13–4 pm, two (2.5%) between 17–20 hours, and seven (8.75%) after 20 hours. Edema was documented at 76/80 (95%), pain at 58 (72.5%), local bleeding at 23 (28.8%), emesis at 10 (12.5%), bullae formation at 8 (10%), and tissue necrosis at three (3.8%) points. Complications presented by level keracunan, lebih sering terjadi pada kasus yang parah: infeksi luka terjadi pada 14/58(24,1%) dengan keracunan	Q1

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	Valverde-Muñoz, María L.Ávila-Agüero (Brenes-Chacón <i>et al.</i> , 2019)	sedang dan 5/5 poin dengan keracunan parah ($p < 0,0001$), bleeding occurs in 3/58 (5.2%) with moderate cases, and 2/5 (40%) in patients with severe poisoning ($p = 0.004$); and compartment syndrome occurred at 3/17 (17.6%) points with mild poisoning, at 33/58 (56.9%), and 5/5 points of moderate and severe poisoning ($p = 0.0014$, respectively). Sequelae documented 25/80 (31%).	
2	TREATMENT OF TIBIAL PSEUDARTHROSIS SECONDARY TO SNAKE BITE IN PEDIATRIC AGE: CHAARIA MISSION HOSPITAL COLLABORATIVE EXPERIENCE G. Gaido, D. D'Aquila, L. Maltesi, L. Cara, A. Mbungu and J. Makand (Gaido <i>et al.</i> , 2017)	Postoperative management The limb is immobilized with a femur-podalic cast and the patient receives antibiotic treatment and supportive care until the stitches are removed. Then a circular full cast is applied with a total immobilization duration lasting 45 days, and avoiding heavy loads on the limbs.	Q4
3	Myocarditis Complicating Viper Snake Bite in a Child K. Jagadish Kumar, Srujan, Ashok	shock caused by the cardiovascular effects of toxins that cause myocarditis supported by elevated CPK-MB levels, ECG findings and Echocardiography. The child experiences	Q4
4	Snake bite management in a toddler: a case report in Sumbawa Besar Ferry Liwang, Fitria Nuraeni, Mulya RKaryanti (Liwang <i>et al.</i> , 2021)	Patients are classified as having third-degree toxins based on clinical features, such as severe palpebral swelling and melena. The results of laboratory tests showed severe anemia (Hb 5.3g / dL) and marked coagulopathy (WBCT does not clot, PT 400 seconds, and aPTT 400 seconds). Patients received suboptimal doses of antivenom, but were supplemented with good supportive therapy, all of which produced good results	Q4
5	Limb salvage following snake bite using acute limb shortening	recovery of the entire injury and almost normal gait with minimal orthotic use are achieved. This case is the first described in the literature where Acute limb shortening with secondary limb lengthening has been	Q3

	and secondary lengthening Sameer SharadMahakalkar , ArghyaKundu Choudhury , Madhubari Vathulya ,Tarun Goyal ,Debarati Chattopadhyay (Mahakalkar et al.,2021)	successfully used for limb rescue in snakebite injuries.	
6	Takotsubo cardiomyopathy in a snake bite victim: a case report Kichiro Murase & Kenji Takagi (Murase & Takagi,2012)	The patient was discharged without disability after two months of rehabilitation.	Q3
7	Acute myocardial infarction following a Russell's viper bite: a case report Mahboob Niraj, Jayamalee L Jayaweera, IndunilWGD Kumara and Nirmali WAJ Tissera (Niraj et al., 2013)	The patient has excessive puncture site bleeding but no other manifestations of bleeding. A chest X-ray showed evidence of pulmonary edema. Then asystole occurs, and cardiopulmonary resuscitation is unsuccessful.	Q4
8	Cardiogenic Shock due to Kounis Syndrome following Cobra Bite W. D. D. Priyankara ,1 E. M. Manoj, A. Gunapala,1 A. G. R. M. A. Ranaweera,2 K. S. Vithanage, M. Sivasubramaniam, and E. Snajeeva (Priyankara et al.,2019)	After a few days in the ICU, she was transferred to the medical ward Her ECG was normal and ECHO recurred within a normal week.	Q3
9	Multiple thromboembolic strokes in a toddler associated with Australian Eastern Brown snake envenomation Hamish Smith, MBBS (Hons)*, Dougal Brown, FRANZCR, MBBS	The child recovers well	Q4

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	(Smith & Brown, 2019)		
10	Evaluation of Risk Factors and Follow- Up Criteria for Severity of Snakebite in Children Fesih Aktar, Safak Aktar, Ilyas Yolbas, and Recep Tekin (Aktar <i>et al.</i> , 2016)	Duration of hospitalization (P <0.001), rural incidence (P <0.001), white blood cell count (WBC) (P = 0.002), ratio of aspartate aminotransferase to alanine aminotransferase (AST/ALT)(P=0.010), hypoproteinemia (P = 0.001), hypoalbuminemia (P<0.001), and hypocalcemia (P = 0.005) were significantly higher in the severe snakebite group. The WBC (P = 0.006) and AST/ALT ratio (P = 0.018) were significantly higher on the first day of the snakebite compared to the following days.	Q3
11	Incidence and mortality due to snakebite in the Americas Jean-Philippe Chippaux (Chippaux, 2017)	The incidence averages about 57,500 snakebites per year (6.34 per year). 100,000 inhabitants), resulting in nearly 370 deaths (0.037 per 100,000 inhabitants), with a case fatality rate below 0.6%. However, there is wide variation between countries	Q1
12	Snakebite is UnderAppreciated: Appraisal of Burden from WestAfrica Abdulrazaq G. Habib,Andreas Kuznik,Muhammad Hamza,Maryam I. Abdullahi, Basheer A. Chedi1,Jean-Philippe Chippaux, David A. Warrell (Habib <i>et al.</i> , 2015)	In West Africa, annual snakebite deaths and amputations range between 24 (95% Confidence Interval: 19–29) and 28 (17–48) in Guinea-Bissau with the highest estimates in 1927 (1529–2333) and 2368 respectively; 1506–4043) each in Nigeria. <i>Annual Disability Adjusted Life Years (DALYs)</i> associated with snakebite deaths range from 1550 DALYs (95% CI: 1227–1873 DALYs) di Guinea Bissau hingga 124,484 DALYs (95% CI: 98,773– 150,712 DALYs) in Nigeria. The annual DALYs associated with amputations for both countries are 149 DALYs (95% CI: 91–256 DALYs) and 12,621 DALYs (95% CI: 8027–21,549 DALYs, respectively). Total load SBE is estimated at 319,874 DALYs (95% CI: 248,357–402,654	Q1
13	Clinical Profile and Laboratory Parameters In 1051 Victims of Snakebite from a Single Centre	Of the 1051 cases, hemotoxic bites exceeded 586 (56%) bites neurotoxic 435 (41%). Most of the victims were	Q4

	<p>in Kerala, South India JC Menon, JK Joseph,MP Jose, BL Dhananjaya, OVOommen (J. Menon et al.,2016)</p>	<p>male 706 (70%), 792 (75%) victims aged between 20-60 years, lower extremity bites predominated, 883 (84%). Among laboratory tests, hemoconcentration (>15 gm/dl), low platelets (<100,000 cmm), proteinuria (3+), increased creatinine (>4 mg/dl) and increased d-dimer (>200 µg/ml). Major complications included death in 38 (3.6%) victims, Acute Respiratory Distress Syndrome 20 (1.9%), Failure Acute renal 220 (20.9%), requiring hemodialysis at 110 (10.4%). Ventilator support required in 41 (3.9%) victims and Gangrene was seen in 43 (4%). 891 (85%) patients received ASV with side effects in 379 (37%) with 3 experiencing anaphylaxis. The average dose of antivenom given for neuroparalytic snake bites is 12.26 vials (range 0-32) and 16.79 vials (range 2-52) for bites</p>	
14	<p>A study of snake bite among children presenting to a paediatric ward in the main Teaching Hospital of North Central Province of Sri Lanka Roshini Kilanthy Karunanayake, Dissanayake Mohottalage Randima Dissanayake and Aranjan Lionel Karunanayake (Karunanayake et al.,2014)</p>	<p>There were 24 males and 20 females. The highest number of bites (48%) are in the age range of 6-12 years. Most bites occurred between 6 p.m. and 6 a.m. (59%). The foot is the most frequently bitten place (48%). Of all venomous bites, the humpback-nosed viper (<i>Hypnale hypnale</i>) accounted for the highest number (44%) and Russell's viper (<i>Daboia ruselii</i>) accounted for the second highest number (27%). A large number of venomous bites occur indoors during sleep (22%). Antivenom serum was administered to (39%) venomous bites. Death occurs in (11%) from venomous bites.</p>	Q2
14	<p>A study of snake bite among children presenting to a paediatric ward in the main Teaching Hospital of North Central Province of Sri Lanka Roshini Kilanthy</p>	<p>There were 24 males and 20 females. The highest number of bites (48%) are in the age range of 6-12 years. Most bites occurred between 6 p.m. and 6 a.m. (59%). The foot is the most frequently bitten place (48%). Of all venomous bites, the humpback-nosed viper (<i>Hypnale hypnale</i>) accounted for the highest number (44%) and Russell's viper (<i>Daboia ruselii</i>) accounted for the second highest number (27%). A</p>	Q2

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	Karunanayake, Dissanayake Mohottalage Randima Dissanayake and Aranjan Lionel Karunanayake (Karunanayake et al.,2014)	large number of venomous bites occur indoors during sleep (22%). Antivenom serum was administered to (39%) venomous bites. Death occurs in (11%) from venomous bites.	
15	Adverse Cardiovascular Events after a Venomous Snakebite in Korea Oh Hyun Kim, Joon Woo Lee, Hyung Il Kim, KyoungChul Cha, Hyun Kim, Kang Hyun Lee, SungOh Hwang, and YongSung Cha (Kim et al., 2016)	Nine (13.8%) of the 65 patients had ACVE; myocardial injury (9 patients, 13.8%) including increased high sensitivity troponin I (hs-TnI) (7 patients, 10.8%) or electrocardiogram (ECG) determines ischemic changes (2 patients, 3.1%), and shock (2 patients, 3.1%). Neither ventricular dysrhythmia nor cardiac arrest is observed. The median increase in hs-TnI levels observed in this study was 0.063 ng/mL (maximum: 3,000 ng/mL) and there were no deaths in the ACVEs group. Underlying heart disease was more common in the ACVE group than in the non-ACVE group (p = 0.017). Regarding complications during hospitalization, 3 patients (5.4%) in the group non-ACVEs and 3 patients (33.3%) in the ACVEs group had bleeding (p = 0.031).	Q2
16	Clinical Profile of Snake Bite in Children in Rural India Vinayak Y. Kshirsagar, MD; Minhajuddin Ahmed, MD; Sylvia M. Colaco, MBBS (Kshirsagar et al.,2013)	Of the 162 patients, 98 (60.49%) were men. The bite was vasculotoxic at 147 (90.74%) and neuroparalytic in 15 (9.25%) patients. Bites mainly occur from July to September with 84 (51.85%) bites. Bites were more common in males older than 5 years (89%) with bite marks mainly on the lower limbs in 120 (74.04%) patients. Deaths were reported in patients who reported late to the hospital with a mortality rate of 1.85%.	Q3
17	Study of Clinico-Epidemiological Profile and Outcome of Poisonous Snake Bites in Children Paudel KM, Sharma S (Paudel & Sharma,2012)	Research shows a predominance of snakebites in males (57.3%) with a higher incidence in children over the age of ten years (58%). Most of the poisoning (71.9%) was seen during June, July and August which corresponds to the monsoon season in Nepal. Most of the victims were bitten by unidentified snakes (52%), mostly in fingers &	Q4

		hands (64.6%). Ptosis is observed in all cases of snakebite poisoning. A little less than 1/3rd of children have respiratory distress that requires breathing assistance. The average ASV used is 18.2 vials. The case fatality rate (CFR) was quite high (28.2%) with more deaths in them who have respiratory distress	
18	Factors affecting outcome in children with snake envenomation: a prospective observational study Jhuma Sankar, Rehana Nabeel, M Jeeva Sankar, Leena Priyambada, S Mahadevan (Sankar et al., 2013)	The following admissions were found to be significantly associated with poor outcomes: age, walking >1 km after a bite, vomiting, hemoglobin ≤ 10 g/dl upon entry and snake species (cobra). In the multivariable analysis, only the younger age (adjusted OR 0.85; 95% CI 0.7 up to 0.9), walking >1 km after bite (adjusted OR 57; 95% CI 4.2 to 782) and hemoglobin ≤ 10 g/dl upon admission (adjusted OR 6; 95% CI 2 to 18.2) remained important. Younger age at presentation, anemia (hemoglobin ≤ 10 g/dl) and walking distance after bite may be independent predictors of mortality and morbidity in children with snakebites. These features in snakebite victims require early referral and Management in Tertiary Care Centers.	Q2
19	Comparison of snakebite cases in children and adults R. TEKIN, B. SULA, G. CAKIRCA, F. AKTAR, Ö. DEVECI, I. YOLBAS, M. K. ÇELEN, M. BEKCIBASI, Y.	The work involved 290 patients, 123 of them were children and 167 were adults. The most common bite sites were the lower extremities with 78.9% (n=97) and 63.5% (n=106) in pediatric and adult patients, respectively. All pediatric patients received prophylactic treatment with antibiotics, while 62 (37.1%) adult patients received antimicrobial treatment due to soft tissue infections. The most common complications developing were pulmonary edema in children at a rate of 33.3% (n = 41) and compartment syndrome in adult patients at a rate of 3% (n = 5).	Q2

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20	Childhood osteomyelitis: imaging characteristics Joost van Schuppen & Martine M. A. C. vanDoorn & Rick R. van Rijn (van Schuppen <i>et al.</i> , 2012)	Paediatric radiology plays an important role in the diagnosis of childhood osteomyelitis and can also be used to guide therapy and intervention.	Q1
21	Surgical Management of Snake Envenomation in India Current Perspective Sheeja Rajan T M1(Rajan, 2017)	Long-term consequences of poorly treated snakebite wounds are chronic ulceration, infection, osteomyelitis, joint contractures, arthritis, and marjolin ulcers in wounds that do not heal.	Q1
22	Challenging Diagnosis for the Forensic Pathologist: A Systematic Review Alessandro Feola, Gian Luca Marella , Anna Carfora , Bruno Della Pietra, Pierluca Zangani and Carlo Pietro Campobasso (Feola <i>et al.</i> , 2020)	Microscopically , signs Ischemic and hemorrhagic encephalopathy has been found in six cases out of 56 cases and extensive perivascular demyelination in one case Myocardial hemorrhage has been reported in seven cases out of 56 and changes consistent with myocardial infarction in one case . Signs of rapid failure of the left ventricle are mostly represented by pulmonary edema and congestion. Additional histological findings were hyaline membranes due to alveolar diffusion damage in three cases and extensive microthrombosis consistent with disseminated intravascular coagulation in four cases (7.142%) .	Q1
23	Snakebite as a Neglected Tropical Diseases in Indonesia:A Review Dewi Yuniasih, Ario Tejosukmono, Junaidy Heriyanto (Yuniasih, 2021)	It is estimated that there are cases of snake bites on 5 islands in Indonesia. The most snakebite cases are in eastern Java. Bondowoso itself had 148 cases during March 2015 until May 2016 More than 38% of snakebite victims are farmers. The area most biting is the hands (52%) and the snake most responsible for causing snake bites in Bondowoso is Trimesurus albolabris snake bite causes disseminated intravascular coagulation with increased fibrinolysis after Rhabdophis bite. Patients received two vials (10mL) of polyvalent antivenom (Biosave) diluted in 500mL of normal saline solution on days 7, 8 and 9 after the bite	Q4

Snakebite in Adult Patients and Pregnant Women

Basically, the pathophysiology, symptoms, and diagnosis of *snakebite* in adult patients and pregnant women are the same. However, there are slight differences in management in handling *snakebite* in adult patients and pregnant women.

Antivenom neutralizes poison in fixed quantities. Both children and adults are given the same amount of antivenom because snakes inject the same amount of venom into both adults and children. Antivenoms can be effective as long as the toxin is still active in the patient's body causing symptoms of systemic poisoning. It can persist for days or even weeks after the bite (Babangida & Baraya, 2020); (Martín-Gutiérrez et al., 2017). The difference between giving pain to adults and pregnant women is given the same. At a dose of paracetamol size 1-4 grams within 24 hours (Babangida & Baraya, 2020).

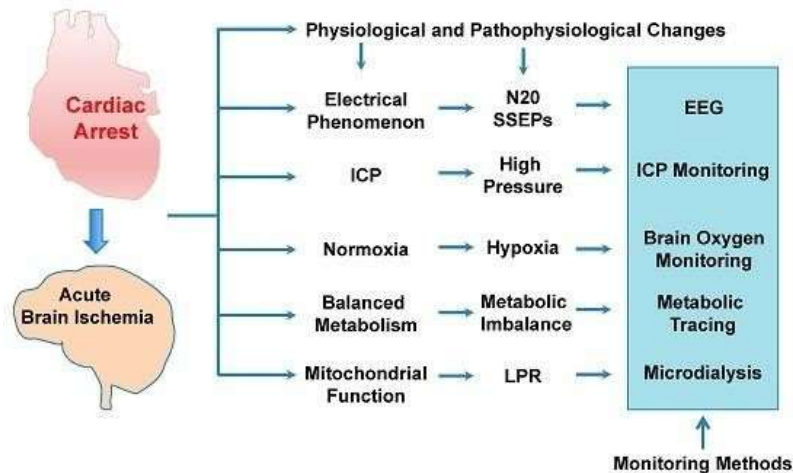
Effects of Snakebite with Osteomyelitis

In developing countries snake bites can cause necrosis and osteomyelitis, with consequent deformities, especially in children (Blandino et al., 2017). Gangrene, osteomyelitis and hypopituitarism are the only long-term complications associated with snakebites in victims (Menon & Joseph, 2015).

After being bitten, local swelling is usually detected within 2-4 hours and can expand rapidly until it reaches its peak on the second or third day. *Blistering* appears within 2-12 hours, and tissue necrosis becomes apparent within 1 day after the bite. Necrotic tissue exfoliation and secondary infection (Resiere, Resiere, et al., 2020). The long-term result of poorly treated snakebite wounds is osteomyelitis in wounds that do not heal (Rajan & Menon, 2017).

Relationship of Snakebite with Hemodynamic Disorders of the Heart

According to Babangida (2020), hypotension and hypovolemia secondary to extravasation of plasma volume in bitten limbs, cause external or invisible blood loss, emetic symptoms due to sympathetic nerve disorders or fears such as persistent vomiting, and failure of adequate oral fluid intake.



Gambar 2. Cardiac Arrest on Snakebite (MDPI, 2022)

Direct cardiovascular effects of toxins such as inhibition of physiological vasomotor systems such as angiotensin-renin-bradykinin systems due to snake venom and sometimes cause anaphylactic effects triggered by antivenom (Javier et al., 2023). The effects of snakebite also affect ions and electrolytes such as potassium which affect the rhythm and contraction of the heart (Javier et al., 2023). A few hours after the bite can cause *cardiogenic shock* and cardiac arrest due to hyperkalemia in patients with massive general skeletal muscle damage (rhabdomyolysis) and well-managed cytotoxic effects (Babangida et al., 2020).

Viperid snake venom induces more prominent local signs such as (edema, blistering and necrosis), cardiovascular shock, and acute renal failure. Neurological involvements such as increased salivation, ptosis, breathing, and general paralysis were seen more in Elapidae bites (Aryal et al., 2017).

Research limitations & medical implications

In this study there are research limitations experienced by researchers. Researchers identified limitations including:

1. There are some journals that cannot be accessed in full / Full Text so that the author takes a long time to find journals.
2. The author needs time to collect journals related to the problem to be used as a reference source that is appropriate to the problem.
1. Authors need more time to analyze and understand the contents of the journal and collect journals or books related to the problem to be used as appropriate reference sources.

CONCLUSION

After a series of processes passed, based on the results of research in *Scopus indexed journals* regarding *the systematic "The Relationship of Snakebite with Hemodynamic Disorders of the Heart in Adult Patients and Pregnant Women"* it can be concluded that the majority of journals discuss heart problems and infections, necrosis in muscles and bones related to poisonous snake bites.

In developing countries snake bites can cause necrosis and osteomyelitis, with consequent deformities, especially in children. After being bitten, the condition of local swelling usually appears within 2-4 hours and can expand rapidly until it reaches its peak on the second or third day (Resiere, Monteiro, et al., 2020). The long-term result of poorly treated snakebite wounds is osteomyelitis in wounds that do not heal, especially in pregnant women who experience higher compression.

Direct cardiovascular effects of toxins such as inhibition of physiological vasomotor systems such as angiotensin-renin-bradykinin systems due to snake venom and sometimes cause anaphylactic effects triggered by antivenom. The effects of *snakebite* also affect ions and electrolytes such as potassium which affect the rhythm and contraction of the heart. A few hours after the bite can cause *cardiogenic shock* and cardiac arrest due to hyperkalemia in patients with massive general skeletal muscle damage (rhabdomyolysis) and well-managed cytotoxic effects (Babangida & Baraya, 2020).

The successful treatment of osteomyelitis with *cardiogenic shock* due to *snakebite* complications depends on extensive surgical debridement and adequate and effective antibiotic therapy. Empirical antibiotics may be given after collecting culture samples in non-septic patients. The duration of antibiotic therapy varies from four weeks to six months, and treatment should be adjusted based on the results of the cultures collected, In cases of acute infection can be treated with antibiotic therapy lasting four to six weeks. Chronic infections should be treated with extensive surgical debridement and removal of synthetic material, this can be collaborated with bone replacement procedures if orthopedic indications are appropriate. Due to the formation of biofilms, the total time of administration of antibiotics in this infection is three to six months.*al., 2014).*

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