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Bitis arietans bite poisoning in Angola regarding a clinical case with compartment syndrome

Paula Regina Simões de Oliveira, Nelson Baldaia, Cerezo H Gaspar, Jéssica Campos, Jose B Silva

ABSTRACT

Introduction: Snake bite poisoning is a serious medical condition and a frequent medical-surgical emergency, which primarily affects rural communities in Africa, Latin America, Asia, and New Guinea. Throughout Southern and Eastern Africa, *Bitis arietans* is responsible for the majority of cases of serious poisoning and death. This article aims to present the first published clinical case that occurred in Angola regarding compartment syndrome caused by a *Bitis arietans* bite.

Case Report: The patient presented compartment syndrome of the right upper limb and profuse bleeding from the bite site with flexural lesions at the level of the forearm, limited movement, and painful palpation. Thumb with bleeding punctuates lesion and blackened skin, asymmetrical chest due to increased volume of the right pectoral region, painful on palpation and without subcutaneous emphysema. After a period of 92 days in hospital and undergoing 9 surgeries, the patient evolved satisfactorily, despite prolonged stay, with surgical approximation of the edges of the surgical wound and it was decided to discharge him for follow-up in surgery consultation.

Conclusion: The multivariate spectrum of clinical complications developed and presented in this case demonstrates that snakebites have unique characteristics that make their prevention and control challenging. Inaccessibility to differentiated healthcare tends to increase complications and the probability of death, when combined with the fact that antivenom is not produced or available in our country. In Angola, snake bites are not a notifiable disease, which makes it difficult to know the statistics of the problem.

Keywords: Angola, *Bitis arietans*, Compartment syndrome

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INTRODUCTION

The World Health Organization reported an incidence of snakebites that is around 5.4 million cases annually, with 2.7 million poisonings, 81,000 to 138,000 deaths and at least 400,000 cases suffering physical and psychological sequelae [1, 2], and considers them to be one of the most neglected and severe public health problems affecting communities in regions where venomous snakes exist. The morbidity and mortality resulting from poisoning is relevant mainly in tropical and subtropical regions of the world [3], constituting an underestimated problem particularly in African countries where the incidence and lethality of these poisonings do not correspond to reality, representing an important problem of Public Health [4, 5].

Snake bite poisoning is a serious medical condition and a frequent medical-surgical emergency, which

primarily affects rural communities in Africa, Latin America, Asia, and New Guinea [5, 6]. They cause a high number of victims that can lead to death, especially in rural areas, where communities suffer most due to living far from health services that are generally inadequately equipped to deal with these medical emergencies [7]. Limb amputation is one of the serious consequences of poisoning, with local and systemic complications being more frequent in children than in adults [8], resulting in permanent weakness and death [9] which affect around 3% of victims [10].

The socioeconomic impact is high on the poorest populations living in rural and tropical areas of Africa, Asia, Oceania, and Latin America, causing morbidity, mortality, and social suffering [11].

Among African snakes, *Bitis arietans* is the species that causes more bites and deaths in humans and dogs than all other species [12], followed by: Najas, Echis, and Mambas (*Dendroaspis* spp.) [4, 5, 12].

Bitis arietans snake belongs to the Viperidae family. It has a relatively thick body with flat head and upward-facing nostrils. It is a snake with a heavy body and a length that can reach 1.4 m, and can come in various colors ranging from black, brown, reddish, or even orange [13]. In Angola they can be found more frequently in Cabinda and in the regions south of the Cuanza River. In the study by Oliveira and Castro [14] its existence was also recorded in Mufuma, Selela (Calandula), and Cuanza Sul (Figure 1).

Studies report that it presents the most toxic venom of the Viperidae family in Africa, as assessed by the average lethal dose (LD50) [15], whose value in mice varies from 0.4–2 mg/kg intravenously (iv) and 4.4–7.7 mg/kg subcutaneous (sc) [16].

From a medical point of view, the World Health Organization (WHO) categorization classifies them as belonging to category 1, which is of great importance, highly poisonous, and can cause high morbidity, disability, or mortality [17].

The most important components of snake venom that cause serious clinical effects are polypeptide toxins, pro-coagulant enzymes, cytolytic toxins, necrotic, hemolytic, myolytic toxins, and pre- and post-synaptic neurotoxins and hemorrhagic toxins, with 79 venom proteins having been isolated from this species [18]. Snake venoms vary in their composition from one species to another, but also within a single species. There are also factors that contribute to this variability, from geographic distribution, diet, different seasons, as well as age [17–19].

Clinically, after a bite by *Bitis arietans*, there is often marked edema that generally extends over the entire limb and spreads to the trunk. There is marked plasma extravasations that can cause hypovolemic shock, a common presentation characteristic of this condition. At the site of the bite, necrosis occurs, which can be extensive, requiring, in some cases, the amputation of part or even the entire affected limb [20].

Systemic symptoms can be early and dramatic with cardiovascular abnormalities, including hypotension and shock, arrhythmias, and electrocardiographic changes [21].

Major arteries may become thrombosed in the bitten limb and rarely at other points. A compartment syndrome can develop, which is rare and characterizes severe cases, being difficult to handle clinically due to the need to measure intra-tissue pressure, when possible, constituting a frequent cause of amputation in several regions of Africa [22]. This syndrome results from the compression of the vascular-nervous bundle, with consequent extensive edema in affected limb and extremities' ischemia. The most important manifestations are intense pain, paresthesia, decreased temperature of the distal segment, cyanosis, and motor deficit [17]. Spontaneous systemic bleeding is common and mediated by the action of zinc-dependent metalloproteinase's (SVMPs), while hemostatic changes include thrombocytopenia and evidence of thrombin-like activities [6, 17].

Compartment syndrome is uncommon, under-diagnosed and requires urgent attention. The clinical appearance of snake-bitten limbs often suggests that a compartment syndrome exists, as it causes intense pain, tense edema, cold skin, absence of nociceptive sensitivity, and a filiform pulse. However, these appearances can be misleading, and when measuring intra-compartmental pressure directly (e.g., with a Stryker monitor), the pressures are considered to be below the danger threshold for ischemic necrosis of intracompartmental muscles [18]. However, if compartment syndrome is suspected, pressure must be measured directly, as it is the only reliable way to confirm it, justifying surgical intervention with fasciotomy. Normal intracompartmental pressure is 0–10 mmHg. An intracompartmental pressure greater than 45 mmHg is generally associated with compartment syndrome [17].

However, animal studies have shown that fasciotomy is ineffective when sparing poisoned muscles [21]. As long as antivenom is administered appropriately and as quickly as possible after the bite, fasciotomy is rarely necessary [17]. However, bites involving the finger pulps are often complicated by necrosis, and a specialist surgeon should be called for further evaluation.

The administration of antivenin has become the therapy of choice in cases of poisoning caused by snake bites. Anti-venoms are produced in animals, usually horses, but also in sheep, after administering snake venom to the animals and subsequently collecting blood, separating the plasma or serum and fractionating it to obtain immunoglobulins, or fragments of immunoglobulin F(ab'2) or Fab [17, 20].

The most important and urgent decision to be made regarding any patient bitten by a snake is whether anti-venom, the only specific antidote to the venom, should be administered [17, 20].

Administration of antivenom is indicated in all cases with clinical signs of systemic poisoning [neurotoxicity, spontaneous systemic bleeding, incoagulable blood (20MWBCT), and cardiovascular changes: hypotension,

shock, arrhythmia, and electrocardiogram abnormalities] or severe local effects (extensive edema involving more than half of the bitten limb, rapid and progressive edema, and bites on fingers and toes) [17, 20].

CASE REPORT

A 42-year-old black man, employee of the prison services of Calumbo (Province of Bengo), who was the victim of a snake bite identified by photography (Figure 2) (*Bitis arietans*) on the back of his right hand between the thumb and index finger, at around 7:00 pm on 09/15/2022, with an initial medical approach at Hospital do Bengo, where volume replacement was performed with 0.9% saline solution and subsequently transferred to the emergency department of the Main Military Hospital where he arrived at around from 9 p.m.

Upon admission, the patient had a Glasgow score of 15 points, reporting pain of 8 points on the numerical pain scale across the entire length of the right upper limb (RUL). On objective examination, distal cyanosis of the right upper limb was highlighted absence of brachial, radial and ulnar pulses. Functional impotence of all fingers, could not perform flexion or extension movements of the fingers, along with increased volume of the right upper limb extending from the distal end to the middle 1/3 of the arm, a bleeding point on the medial surface of the thumb, and pain upon palpation (Figures 3 and 4). Evaluated by a surgeon who decided to take the patient to the operating room, where an enlarged fasciotomy was performed on the right forearm, passing through the skin, subcutaneous cellular tissue (SCT) to the palmar fascia, with control of hemostasis, extensive washing with hydrogen peroxide and physiological saline solution (Figures 5 and 6).

He was later admitted to the Intensive Care Unit (ICU) (09/16/2022). On admission with Glasgow of 15 points, without motor deficit; hemodynamic stability without vasopressor drugs MAP (95 mmHg); asymmetrical chest due to increased volume of the right pectoral region, painful on palpation and without subcutaneous emphysema. Preserved chest expansion, spontaneous breathing in room air, with SpO_2: 100%, RR: 12 cpm. Chest and abdomen without changes; Upper limbs, asymmetrical due to increased volume of the right upper limb, with flexural lesions at the level of the forearm, limited movement and painful on palpation. Thumb with bleeding punctate lesion and blackened skin, surgical dressing covered with hematic secretion, lower limbs symmetrical and without edema. Blood gas analysis upon admission to the ICU (FiO_2: 0.21%); pH: 7.46; $paCO_2$: 36 mmHg; paO_2: 90 mmHg; SaO_2: 97%; HCO_3: 25.6 mmol/L; Base excess: 1.8 mmol/L; Na_+: 133 mmol/L; K_+: 4.9 mmol/L; Ca_+: 1.08 mmol/L; Glycemia: 150 mg/dl; lactate: 0.8 mmol/L; Hb: 9.3 g/dL; Hto: 30%. Blood count: Hb: 9.2 g/dL; Hto: 26.9%; Platelets: 297 × 10 9/L; Leukocytes: 20.11 × 10 9/L; Neutrophils: 86.6%; Lymphocytes: 8.6%. Biochemistry of liver and kidney function: Total bilirubin: 0.65 mg/dL; Direct bilirubin: 0.22 mg/dL; Oxaloacetic transaminase (OAT): 45.0 U/L; Glutamic pyruvic transaminase (GPT): 25.5 U/L; Creatinine: 1.0 mg/dL; Urea: 44.94 mg/dL; Bleeding time 15 min, Clotting time 25 min; Activated partial tromboplastin time 65 sec; International normalized ratio 8.

Medicated after 24 hours with antivenin (SAIMR POLYVALENT SNAKE ANTIVENIN—40 mL); empirical antibiotic therapy with ceftriaxone 1 g/2×/day and vancomycin 1 g/2×/day; aminocaproic acid 7.5 g/day; Analgesia with tramadol; hydration with saline solution according to needs. The patient remained in the ICU for 11 days. He continued to bleed on a towel for the first 96 hours, developing anemia (Hb: 5.4 g/dL), requiring a transfusion of 2 units of packed red blood cells. He was taken to the operating room on 4 occasions for dressing under general anesthesia. He evolved with hemodynamic and respiratory stability. Analytically, there is a decrease in infectious markers, with no signs of surgical wound infection. Therefore, it was decided to transfer the patient to the Surgery ward. The fasciotomy wound evolved with few sloughs, necrosis of the subcutaneous cellular tissue, with no purulent secretion escaping. It later evolved with useful granulation tissue, covering the right upper limb (RUL) muscles, but with the presence of a necrotic plaque on the thumb, so a necrotomy was performed (Figures 7 and 8). With the development of useful granulation tissue, which bleeds easily when touched (Figure 9), without slough or purulent secretion, he remained hospitalized for 92 days, having undergone 9 surgeries, surgical approximation of the edges of the surgical wound (Figure 10) was carried out and it was decided to discharge the patient with a follow-up in a surgical consultation.

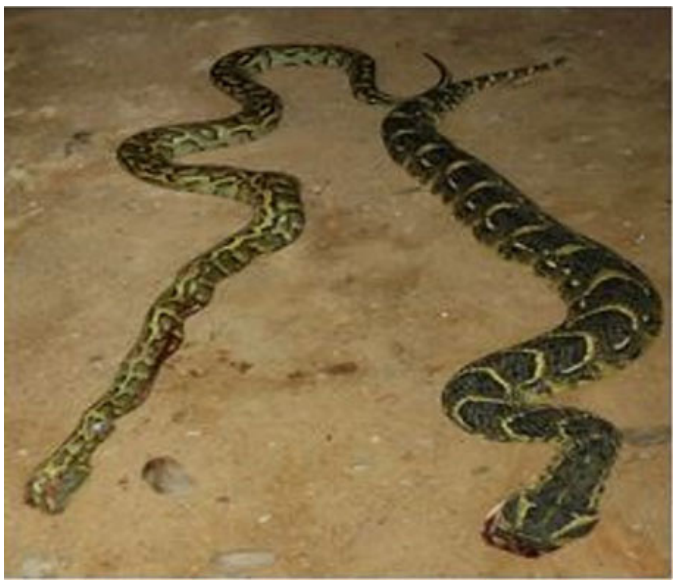

Figure 1: *Bitis arietans* on the right that caused the poisoning described in this article.

Figure 2: *Bitis arietans*'s fangs.

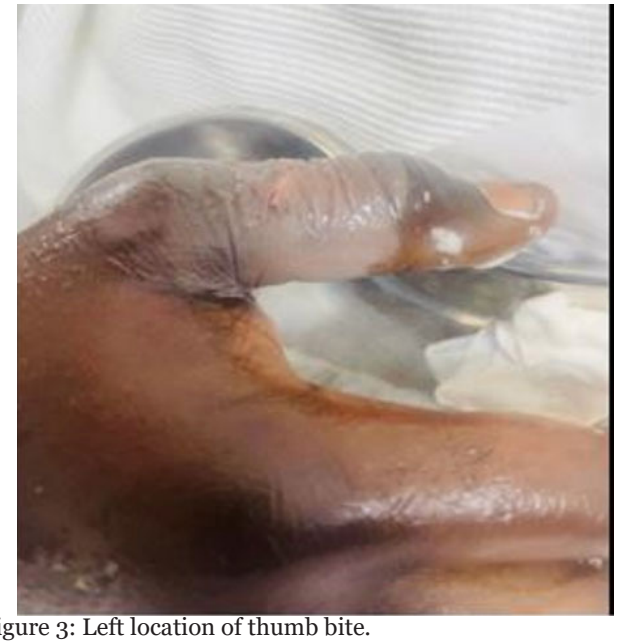

Figure 3: Left location of thumb bite.

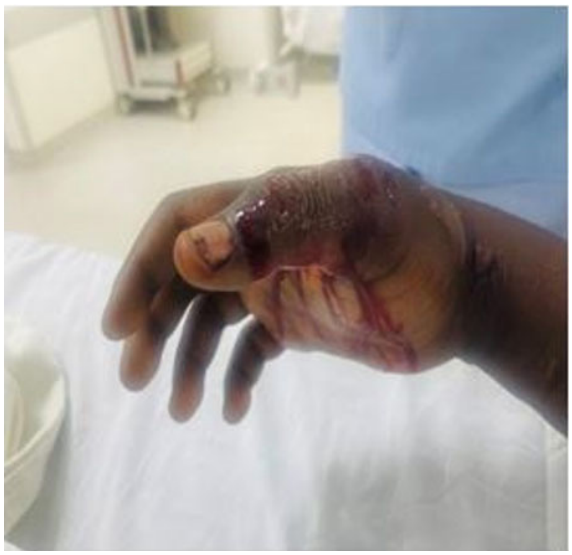

Figure 4: Marked edema of the hand with spontaneous bleeding from the bite site.

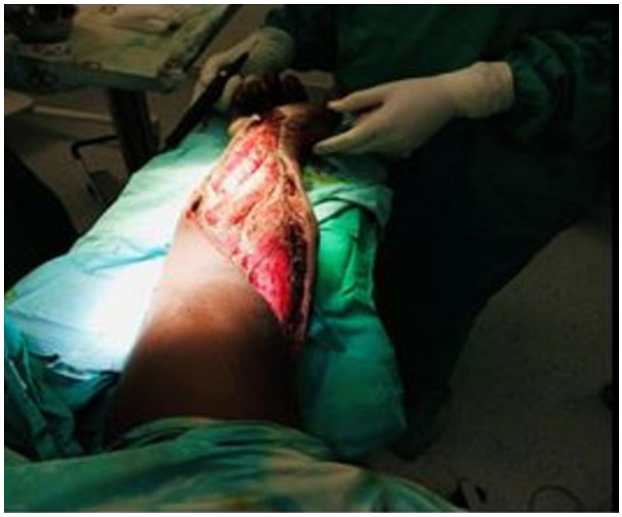

Figure 5: Forearm fasciotomy.

Figure 6: Forearm fasciotomy.

Figure 7: Marked necrosis of the thumb.

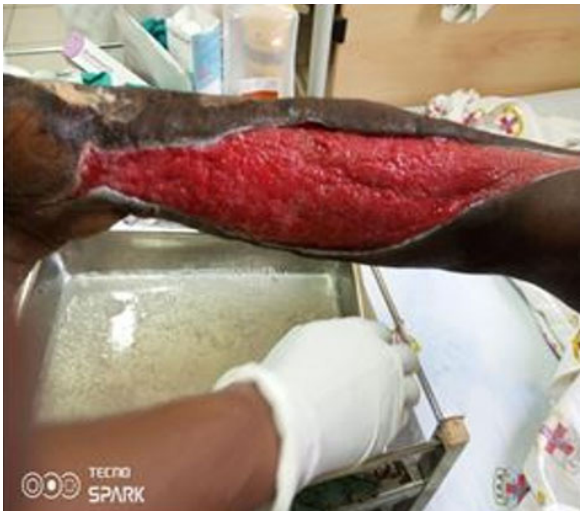

Figure 8: Growth of granulation tissue.


Figure 9: Profuse bleeding after 72 hours.

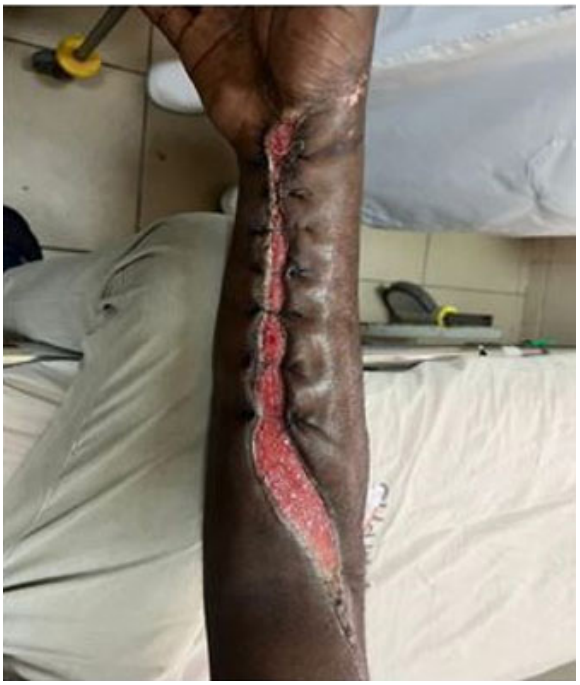
Figure 10: Approximation of the edges of the fasciotomy.

DISCUSSION

Bitis arietans is the venomous snake that causes the most accidents across the African continent, especially in sub-Saharan Africa, probably due to its cryptic color and wide territorial distribution [23–26]. Research reports that it presents the most toxic venom of the Viperidae family in Africa, as assessed by the average lethal dose (LD50) [15], whose value in mice varies from 0.4–2 mg/kg intravenously (iv) and 4.4–7.7 mg/kg subcutaneous (sc) [16].

From a medical point of view, the WHO categorization classifies them as belonging to category 1, which is of great importance, highly poisonous and can cause high morbidity, disability, or mortality [20].

Snake poisoning is a medical emergency that requires immediate attention. The venom of *Bitis arietans* causes serious local and systemic complications, due to the existence of a thrombolytic enzyme that causes tissue necrosis, hypotension, coagulopathy, thrombocytopenia, and spontaneous bleeding [26, 27].

Contrary to what occurred in the case described by Warrell [28], which involved a prick on the middle finger of the left hand that did not present active local bleeding, in our case the active bleeding continued for 72 hours after the fasciotomy was performed, however, similar to what occurred in our case, marked edema was observed on the back of the hand, which expanded to all fingers and progressed proximally to the elbow and axilla and pectoral region, less than 24 hours, with a marked subcutaneous hemorrhage developing in your arm back and chest wall. This last finding in our case was not noticeable due to the color of our patient's skin, which was black, but in the laboratory, he showed signs of coagulopathy with a drop in hemoglobin 9.2 g/dL at entry to 5.4 g/dL, in the first 72 hours after the bite, with the need for transfusion of packed red blood cells [29]. Despite the surgical approach at the appropriate time and treatment with antivenom, the patient's hospital stay was longer than 90 days, which shows the economic impact of snakebites. In the case of Wakasugi et al. [26], the edema peaked on the 4th day and lasted 14 days, with six sessions of 90 min each of hyperbaric oxygen therapy being used, which greatly contributed to the reduction of the arm circumference and the development of compartment syndrome [26]. In Angola, there are currently no hyperbaric chambers in hospitals, so in this case an attempt could be made to intervene as the Japanese colleagues did with the case they described. This adjuvant therapy is strongly recommended by other authors in snakebites to avoid adverse outcomes [30].

In the case described by Lavonas et al. [27], who reported a serious poisoning characterized by marked edema, local tissue necrosis, hypotension, thrombocytopenia, severe coagulopathy, and hemorrhage, had the need to administer 15 vials of polyvalent antivenom from South Africa (150 mL of serum) starting 4–5 hours after poisoning, with gradual improvement in

hematological abnormalities, contrary to what occurred in our case, where only 4 (40 mL) ampoules of serum were administered due to in-hospital unavailability, with the recommended initial dose being 50–100 mL for patients. In a survey of ten patients bitten by this species, carried out by David Warrell in Nigeria [30], he found that six showed severe local signs and four also had systemic signs of poisoning, including spontaneous bleeding with thrombocytoponeia, hypotension, and bradycardia, and recommended that patients with bleeding spontaneous site, more than half of the limb affected with edema or signs of systemic poisoning should receive at least 80 mL of serum [26].

Bitis venom is complex and has several components. One of the components is thrombin-like enzymes (TLEs) [31], which consume fibrinogen and can in turn lead to life-threatening hemorrhage [32]. Thrombomodulin (TM) is a coenzyme that monitors thrombin production on the surface of vascular endothelial cell membranes, retains excess thrombin, and modulates the substrate specificity of thrombin from anticoagulant to antithrombotic. Recombinant thrombomodulin (rTM), developed in Japan for the treatment of disseminated intravascular coagulation (DIC), promotes the activation of protein C by thrombin. Activated protein C (APC) inhibits the production of thrombin by inactivating the coagulation factors Va and VIIIa, thus inhibiting the conversion of fibrinogen into fibrin [33]. Wakasugi's team [26] postulated that rTM would influence this case due to its action on thrombin, having found that there was a decrease in platelet count and mild coagulopathy, but there was no decrease in fibrinogen levels, which suggests that the inhibition of thrombin generation by rTM may have suppressed fibrinogen consumption, therefore, no serious coagulopathy requiring blood transfusion occurred. In our case, it was possible to administer a subdose of the necessary antivenom, which, in conjunction with other procedures, proved to be ineffective. If we consider the prolonged period of hospitalization. The alternative therapy of recombinant thrombomodulin could prove to be an effective therapy [26, 33] to be introduced in Angola since most hospital units do not have antivenom available.

Bitis arietans venom increases vascular permeability to proteins and red blood cells, mainly in the splanchnic regions, leading to hypovolemic shock and death. Our patient also presented severe edema of the upper arm and right hemithorax due to increased vascular permeability and required a large volume of fluid infusion to maintain circulation, as well as fasciotomy and debridement due to the compartment syndrome he presented. Despite the necrosis that the thumb presented, debridements were carried out in order to avoid amputation of the finger. In one of the cases reported by Gras and his team [8], a 13-year-old boy bitten by *Bitis arietans* had an unfavorable local evolution with the necrosis progressing to the hand, requiring amputation and eight surgeries.

From the extensive literature consulted on clinical cases of poisoning with this species, our attention is drawn to the rapid evolution of edema, which in approximately 24 hours can progress from the finger to the upper limb and chest wall, requiring strict control to avoid compartment syndromes as well as a prolonged recovery period, especially in cases where there is a need to perform a fasciotomy due to the same.

CONCLUSION

Bitis arietans poisoning demonstrates that snakebites have unique characteristics that make their prevention and control challenging.

It is imperative to make serum available in health units for the timely and effective treatment of poisonings, thus avoiding prolonged hospitalizations, amputations, and increased morbidity and mortality, which constitute a high cost for the country.

Unlike many infectious diseases, snakebites cannot be eradicated, but their incidence and social impact can be reduced through effective prevention programs, access, and availability of treatment.

It is imperative to engage communities to improve the coexistence of humans, domestic animals, and snakes in rural agroecosystems.

The strategy launched by the WHO in 2019 for prevention and control with the aim of halving deaths and disabilities by 2030 is based on 4 pillars, that is: Involving communities; ensure safe and effective treatment; strengthen health systems; and increase partnerships, coordination, and resources. These must be a priority for Angola.

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Author Contributions

Paula Regina Simões de Oliveira – Conception of the work, Design of the work, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Nelson Baldaia – Design of the work, Acquisition of data, Analysis of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Cerezo H Gaspar – Acquisition of data, Analysis of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jéssica Campos – Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jose B Silva – Design of the work, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission
The corresponding author is the guarantor of submission.

Source of Support
None.

Consent Statement
Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.