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# Epidemiological Aspects and Management of Ophidien Envenimation in Libreville

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## Abstract

**Introduction**: In 2017, WHO reintegrated snake bites into neglected tropical diseases. Our objective was to describe the epidemiological characteristics of ophidian envenomations treated in Libreville from 01/01/2012 to 03/31/2019. **Methodology**: This was a retrospective descriptive multicenter study over 7 years (2012-2018) and prospective (1st quarter 2019) about 23 cases. All patients received for ophidian envenomation with key information for our study were included. Ethical considerations were respected. **Results**: We conducted our study on 23 cases of ophidian envenomation. The median age was 26 years. There was a slight male predominance with a sex ratio of 1.09. Bites were mainly nocturnal 34.78% of cases. The lower limb was most affected 73.91% of cases. Local syndrome was the most common clinical sign. Viperine syndrome accounted for 95.65% of cases. Biological tests were not often requested. Those who had coagulopathy were 26.09% of cases. 01 patient had an ECG. 01 patient died. Out of 23 envenomations, 19 had antivenom. **Conclusion**: The establishment of therapeutic protocols and the accessibility to antivenom will contribute to improving the hospital management of these pathologies.

## Keywords

Antivenom, Envenomation, Snakes, Gabon

## 1. Introduction

Envenomations are a nightmare for humans. According to KASTURIRATNE *et*

*al.*, the number of snake bites would reach 5.5 million per year and these would be responsible for 200,000 to 94,000 deaths per year [1] with approximately 3 times more amputations and permanent disabilities [2]. In 2008, studies estimated that the incidence of ophidian envenomations was 154 per 100,000 people in sub-Saharan Africa and that of deaths per 100,000 inhabitants following ophidian envenomation was 3.85 in sub-Saharan Africa [1] [3]. Most recently, a meta-analysis by Chippaux suggested a 10 times higher envenomation rate in rural areas (75.5 envenomings per 100,000 people) than in urban areas (5.2 envenomings per 100,000 inhabitants). Mortality in urban areas was relatively low (0.06 deaths per 100,000 people) while the annual rural mortality rate was 1.35 deaths per 100,000 [4]. However, the data remain largely underestimated due to patients treated by traditional healers and those who died before arriving at a health facility. Thus, The World Health Organization (WHO) reinstated snakebites in the list of neglected tropical diseases in 2017. One of the points of the resolution voted by the WHO is the desire to strengthen knowledge on the epidemiology of these envenomations, particularly in areas where their incidence is highest, in order to better assess the need for antivenom serum. TCHOUA *et al.* conducted an epidemiological study in Libreville on ophidian envenomations covering the period 1998-2001 [5]. This study had identified 157 patients for ophidian bites, including 27 cases of envenomation. Treatments previously recommended but currently prohibited had been administered to the patients. Indeed, all the envenomed patients had received corticosteroid therapy, 17 patients had received an anticoagulant. However, this study was carried out in an urban environment, in the country's reference medical structure at the time, and therefore could not reflect the real incidence of this phenomenon. More recently, in 2022, a small study, driven in a small rural place in Gabon, showed that the average annual incidence rate of snakebites is around 77 per 100,000 [6]. These data alone on the territory show that the recent epidemiological situation for this pathology is poorly known in Gabon. We proposed to carry out a study with a view to providing recent data on ophidian envenomations in Libreville and their management

## 2. Materials and Methods

We conducted our study at the level of the Emergency Reception Services and in the Intensive Care Units (ICU) of the 02 main University Hospitals and the 02 Army Training Hospitals of Libreville. These were the Army Training Hospitals Omar BONGO ONDIMBA (A.T.H.O.B.O) and Akanda (A.T.H.A), University Hospital of Libreville (U.H.L), the University Hospital of Owendo (A.T.H.O). This was a multicenter observational study with a descriptive aim in two phases: retrospective (01/01/2012 to 31/12/2018) and prospective (01/01/2019 to 31/03/2019) were included all patients admitted to the emergency and intensive care units of the four university hospitals in Libreville for snake envenomation with the presence of viper syndrome (local syndrome, hematological disorders) or cobra syndrome (muscarinic syndrome, cranial nerve and respiratory muscle paralysis, etc.)

during our study period and with records containing the essential information for our study: Patients with an envenomation grade of at least 1 point were selected for the study (Table 1).

We have not included, patient with incomplete medical records concerning the essential information for our study (retrospective section); and those who refused to sign informed consent (prospective section). The variables studied included

- Sociodemographic data: location of treatment, age, sex, snake involved, time of day of bite, geographic location of bite, and pre-hospital care pathway;
- Clinical data: anatomical location of bite, local syndrome, bleeding, hypotension, acute pulmonary edema, shock, eyelid ptosis, level of consciousness, and gastrointestinal signs; The existence of clinical signs or their progression was reassessed every hour by monitoring and measuring the perimeter of the bitten limb;
- Laboratory data: coagulopathy (PT, APTT, fibrinogen, platelet count), renal function (urea nitrogen, serum creatinine);
- Severity: clinical and laboratory grade of envenomation (see Table 1);
- Type of syndrome: viper syndrome (local syndrome, hematological disorders), cobra syndrome (hypersalivation, miosis, bronchial hypersecretion, eyelid ptosis);
- Care provided outside a healthcare facility;
- Therapeutic management: antivenom administration, type of antivenom, adverse effects of the antivenom, admission to the ICU according to grade, adjuvant treatments;
- Patient outcome: length of hospitalization, sequelae, and deaths.

Patients lost to follow-up, who requested to leave the study, or for whom the possible administration of SAV was not reported were excluded from the study.

The data collection for the retrospective portion, were collected based on information collected in patient files from the department's hospitalization records. For the prospective portion, data were collected using a previously established individual data collection form. The data were then entered into a computer and analyzed using © Epi-info software, version 7.1.5.2. The tables were generated using © Excel 2013.

The study received approval from the management of the university hospitals surveyed. For the retrospective portion of this descriptive study, no consent was required. The providers present at the time of the survey were simply asked for authorization to search and analyze the records. Data confidentiality was preserved during the research of essential data or their analysis. For the prospective portion, the investigator was authorized to observe care without intervention, after signing an informed consent form, which is required for each patient included in the study. For this consent, each patient was informed that their participation in the study was voluntary and that refusal to participate would have no impact on the care provided. For the patients who were included, this purely descriptive study, not interfering with the quality of care administered, the risks linked to this

work were considered zero.

**Table 1.** Clinical-biological gradation of envenomations.

| Grade | Viper syndrome | Hemorrhagic syndrome | Neurotoxic syndrome (muscarinic/cobraic) | Laboratory signs | Management |
|---|---|---|---|---|---|
| **0** | - Minimal pain<br>- Hook marks<br>- Local swelling<br>- Circumscribed bruise | - No bleeding | No signs described by the patient | Normal TCTS Normal fibrinogen Normal platelets | Disinfect the wound VAT-SAT Monitor for 4 hours |
| **1** | Severe pain<br>- Localized swelling not extending beyond the adjacent joint | Local bleeding persisting for more than one hour | - Local anesthesia<br>- Tingling, tingling in the bitten limb<br>- Skin muscle fasciculations in the bitten limb | - Normal TCTS<br>- Platelets 150 10-3 per mm3<br>- Fibrinogen > 1.8 g/L | Same as grade 0+<br>- Antivenom<br>- Hospitalization and monitoring<br>- Symptomatic treatment |
| **2** | - Progressive edema not exceeding two adjacent joints | - Mucosal bleeding<br>- Bleeding from old scars | - Muscarinic syndrome (vomiting + excessive sweating + increased salivation + diarrhea + miosis) | - Leukocytosis<br>- Platelets < 150 10-3/mm3<br>- Prothrombin time < 50%<br>- Fibrinogen < 1.5 g/L<br>- CPK < 200 IU/L<br>- D-dimer < 500 mg/L | Same as grade 0+<br>- Antivenom<br>- Hospitalization and monitoring<br>- Symptomatic treatment |
| **3** | - Extensive edema not extending beyond the root of the limb | - Extensive bruising<br>- Distant hematomas<br>- Purpura<br>- Distant blisters | - Cobra syndrome<br>- Tinnitus, phosphenes, dysgeusia<br>- Bilateral palpebral ptosis<br>- Rictus (mouth paralysis)<br>- Dysphagia<br>- Dyspnea | - Anemia<br>- Leukocytosis<br>- Platelets < 150 10-3/mm3<br>- Prothrombin time < 50%<br>- Fibrinogen < 1.5 g/L<br>- CPK < 200 IU/L<br>- D-dimer < 500 mg/L | Same as grade 0+<br>- Antivenom<br>- Hospitalization and monitoring<br>- Symptomatic treatment |
| **4** | - Edema extending beyond the root of the limb (anasarca) | - Internal hemorrhage (peritoneal, meningeal)<br>- Acute anemia | - Flaccid motor paralysis<br>- Communication impossible<br>- Respiratory distress | Same grade 3 | - Place in intensive care Antivenoms |

## 3. Results

During the study period, we recorded 23 cases of envenomation out of 41 cases of snake bites. The average age of the population studied was 27.10 years with extremes ranging from 08 to 54 years. The median age was 26 years. The sex ratio (M/F) was 1.09.

The snake was seen by the victim in 30.4% of cases, or 07 patients. The bites were mainly nocturnal, but the time was not specified in nearly 47.8%, and occurred in a semi-urban environment in nearly 60.9% of cases.

The average time to treatment at the university hospital centers was 16 hours, with extremes ranging from 30 minutes to one week. The median of this treatment time was 02 hours.

The bite involved the lower limb in 73.9% of cases.

The main clinical signs related to envenomation were represented by the local syndrome (pain, edema, traces of hooks) in 91.3% of cases. At the hemodynamic

level, one case of hypotension, 2 states of shock and 2 cases of acute pulmonary edema were found.

At the neurological level, one case of ptosis and impaired consciousness was collected among the included population.

On the hematological level, coagulopathy was found in 26.1% of cases.

Digestive signs consisted of nausea, hypersalivation, vomiting, diarrhea and abdominal pain. Digestive signs were present in 08 patients, or 34.8% of cases.

The grade of envenomation was established according to the current clinical-biological grading. In the absence of the results of biological examinations, clinical gradation was preferred. The distribution of cases according to the grade of envenomation is shown in Table 2.

Table 2. Distribution of cases according to the grade of envenomation.

| Grade of envenomation | Number (n) | Percentage (%) |
|---|---|---|
| 1 | 06 | 26,1 |
| 2 | 12 | 52,2 |
| 3 | 05 | 21,7 |
| **Total** | **23** | **100,0** |

Viper syndrome was present in 22 patients, or 95.6% of cases, compared to 01 case (4.3%) of cobraic syndrome (hypersialorrhea, miosis, bronchial hypersecretion, eyelid ptosis).

Concerning management, antivenom was prescribed and administered to 19 patients, or 82.6% of cases. It was not administered to 4 patients. The type of antivenom prescribed was FAV Afrique® and Inoserp panafricain®. A total of 33 prescriptions (1 ampoule per prescription) were made, including 13 of SAV FAV Afrique® and 20 of SAV Inoserp panafricain®. Adverse effects related to the injection of antivenom serum were found in 01 patient.

All patients were initially admitted to the emergency departments. Six of them were admitted to an intensive care unit. Of this number, 03 patients were at grade 3 of envenomation, 02 patients at grade 02 and 01 patient at grade 01.

The duration of hospitalization was recorded in 10 medical records. It varied between 01 and 07 days, with an average length of stay of 3 days. We recorded 01 cases of death.

## 4. Discussion

Our study is a retrospective study with a weak prospective component. Although its retrospective component is already a limitation, a selection bias exists due to poor archiving and missing information in the medical records. For example, the recurring absence of additional examinations (TP, TCA, fibrinogen, CBC, creatinine) useful for the precise categorization of the grade of envenomation. The multicentric nature, although a strength, had limitations due to the low representa-

tiveness of the CHUO and HIAA samples. The creation dates of these two structures (2016 for the CHUO and 2018 for the HIAA) did not allow us to recruit patients from 2012 to February 2016 for the CHUO and from 2012 to April 2018 for the HIAA. In addition, the small sample of our study population may not be representative. Furthermore, the study took place almost exclusively in an urban environment, known to have fewer snake bites. In fact, the frequencies and incidences of envenomation cannot be extrapolated to the general population [6]. However, the multicentric nature and the long duration of the study allow us to draw conclusions from our study and compare it to those of other authors.

The frequency of snake envenomations was 53.1% (23 envenomations for 41 snake bites). Indeed, not all bites are necessarily followed by venom injection and not all snakes are venomous. Venom inoculation is a voluntary act of the snake [7]. Snake bites are most often accidental and the snake only bites to defend itself. The proven ineffectiveness of certain practices (application of tourniquets, scarifications, etc.) is masked by the high frequency of so-called "dry" bites.

We found a median age of 26 years with a predominance of the 26 to 45 age group constituting the most active population. TCHOUA R *et al.* also found a predominance of young workers [5]. CHIPPEAUX JP *et al.* in Cameroon and LARRECHE S in Djibouti found a predominance in the age groups of 15 to 44 years [8] and 21 to 40 years [9] respectively. LAM A *et al.* in Senegal found a median age of 22 years [10]. All these studies confirm that this age group constitutes the most exposed population. In the study, there is practically no predominance of one sex over the other. This parity is also found in TCHOUA R *et al.* in Gabon who found equality between the two sexes [5]. The risk of envenomation is therefore not a function of sex. However, LAM A. *et al.* found a clear male predominance (73%) in their study in Senegal [10]. This can be explained by the fact that the Senegalese study was conducted on an agricultural population. This activity is mainly male in this country, hence a predominant exposure of men.

In the majority of cases, the snake was not seen (69.6%). The lack of visualization of the snake could be explained by the fact that most of the bites were made at night, peak activity of snakes, especially nocturnal crotalines [11]. In addition, snakes most often bite only to protect themselves, and usually flee after the bite.

The majority of bites occur in the semi-urban environment. The semi-urban environment is the result of anarchic urbanization. This could favor a habitat for snakes and rodents that are their food.

The anatomical location of the bite was mainly on the lower limb, or 73.9% of cases. The predominance of bites on the lower limb was also noted in the studies of TCHOUA R *et al.* in Gabon with 89% of cases [5], HECKMANN X in Guyana with 80% of cases [11], DRABO Y J in Burkina Faso with 70% of cases [12] and TAJELLIJITI in Morocco with 60% of cases [13]. The snake being a reptile living most often on the ground, this could justify the preponderance of bites at the level of the lower limb.

The cobra syndrome was represented in 01 patient. It was a snake trainer who

had a "work accident". He presented with hypersialorrhea, bronchial hypersecretion, miosis associated with bilateral eyelid ptosis. TCHOUA R *et al.* had not found any cases of cobra syndrome [5]. The rapidity of the lethality of the cobra syndrome could explain the low incidence of this syndrome in our study. The viper syndrome was present in 95.6% of patients. Indeed, viperids are the most numerous in Africa.

Hematological signs, in this case blood clot disorders, are the prerogative of viper syndrome. It can be recognized by physical signs, such as bleeding at the bite site, bleeding other than at the bite site (hematuria, epistaxis, hemoptysis, digestive bleeding, etc.). In the absence of a functional laboratory, The Whole Blood Clot Test can help to grade the level of envenomation. Finally, biological tests, especially CBC, TP, TCA, fibrinogen are fundamental tests to classify the grade of viper envenomation, but also to monitor the evolution of hematological disorders. They should be performed early, because biological disturbances precede clinical manifestations. The Whole Blood Clot Test was never performed in our study. The failure to perform this test, which is simple, easy to perform and inexpensive, could reflect a lack of awareness of this test among healthcare providers. The rare biological tests mentioned above allowed us to note 26.09% of cases of coagulopathy. The study by THOMAS L. in Martinique found 23.44% of coagulopathy through his study on coagulation disorders induced by the viper *Bothrops Lanceolatus* [14] while MION G *et al.* in theirs, found 50% of hematological disorders [15]. Their study focused on envenomations by the viper *Echis* which is known for its venom which causes hemorrhages. Digestive signs were present in 34.78% of patients. TCHOUA R *et al.* found 22% of digestive signs [5]. Similarly, SORKINE M. found the frequent presence of digestive signs in his study [16]. The interpretation of these signs must be done with caution, because they can be caused by a state of stress. But in the event of envenomation, they sign at least a grade 2, which justifies the immediate administration of the antivenom.

The antivenom was prescribed and administered to 19 patients. It was not administered to 4 patients. These results could reflect the lack of knowledge of the clinical signs of envenomation and the resulting treatment protocols by healthcare providers. Unfortunately, it is sometimes the difficulty in obtaining the antivenom by healthcare facilities and/or by the patient that remains a major factor in non-treatment. Pharmacies only have antivenom in limited quantities and at prices that are sometimes beyond the reach of the average citizen. An ampoule of the antivenom, Inoserp panafricain® costs on average around 75,000 FCFA in pharmacies in Libreville, or half the country's minimum wage.

Two antivenoms were regularly prescribed, namely Inoserp panafricain® and FAV Afrique®. Inoserp panafricain® was more prescribed (60.6%) than FAV Afrique®. This could be explained by the fact that in 2014, the pharmaceutical laboratory Sanofi® stopped the production of SAV FAV Afrique® [17]. In addition, Inoserp panafricain® is a lyophilized SAV that better corresponds to the storage conditions in tropical environments and covers more species of snakes.

The average length of hospitalization was 03 days with extremes ranging from 01 to 07 days. LAM A *et al.* found a length of hospitalization of less than 02 days (42 hours) [10].

In the study, a 19-year-old patient died in a picture of acute pulmonary edema, associated with hemoperitoneum during her observation period. She was observed for 12 hours without being able to benefit from antivenom. On the other hand, grade 1 patients who did not receive antivenom did not have a life-threatening prognosis.

This observation could support the approach of AUBRY P. *et al.* who recommends the use of SAV only from grade 2 envenomation [18]. The poverty of the African population, the expensive nature of SAV and the practice in a hospital environment could be more suitable for the application of this recommendation.

## 5. Conclusions

Snake bites, re-listed in 2017 in the list of neglected tropical diseases by the WHO, are a public health problem. The epidemiological and clinical profile of ophidian envenomations has not changed much since the original study by TCHOUA R *et al.* (1998-2001) to the present day. Better patient care inevitably requires the implementation and rigorous monitoring of therapeutic protocols in the various departments responsible for the management of this pathology and better availability of antivenom serums.

Recognition of signs of envenomation is essential. The systematic performance of the Whole Blood Clot test should be known and applied, as well as the prescription of certain biological tests which should be systematic (NFS, TP, Fibrinogen, TCA). Finally, more should be done to raise public awareness about the correct actions to take in the event of a snake bite. Health workers should make an effort to better educate themselves on this pathology and, above all, ensure that medical records are properly maintained to facilitate future studies on the issue. These additional studies should provide the necessary epidemiological data so that the WHO can finally take the correct measure of the problem and support the various countries affected by this disease.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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