Perspectives from MSF snakebite programme implementation in Agok, Abyei region, South Sudan

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Abstract

Introduction: Snakebite is a neglected tropical disease affecting around five million people, causing more than 100,000 annual deaths, as well as serious disabilities; however, access to antivenom and high-quality programmatic care remain a global challenge.

Objective: Due to the high burden of snakebite in South Sudan and the serious negative outcomes if left untreated, Médecins Sans Frontières (MSF) integrated snakebite care for the first time among its priorities and consolidated a programme in Agok Hospital.

Method: We describe the history, implementation, and challenges of the MSF snakebite programme.

Results: The number of snakebite patients at MSF Agok Hospital has increased each year. From 2013 to 2019, MSF treated 2,005 snakebite patients. In 2019 there were 527 snakebite admissions, 47% presented with severe envenomation, and one death. Puff adders, vipers and various cobras were identified. Agok Hospital gained understanding on the barriers and facilitators for the population to access care after a snakebite. MSF developed "snakebite diagnosis and treatment" algorithms, and provided clinical training, with the validation of national health authorities. Preventive activities were reinforced. Integration of surgical services was an essential programmatic aspect to monitor and treat complications. Challenges for implementation included a lack of easily available antivenoms in the international market. and the need of a strong supply chain and procurement systems.

Conclusion: The delivery of healthcare towards snakebite patients can be successfully implemented when prioritized. Global efforts to improve access and quality of antivenoms and snakebite care could help removing Snakebite Envenoming from the Neglected Tropical Diseases list.

Keywords: snakebite, snake, envenoming, antivenom, implementation, humanitarianism, secondary care, South Sudan

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Introduction

Global and national burden

Every five minutes, somebody dies from a snakebite. According to the World Health Organization (WHO), an estimated 5.4 million people get bitten worldwide every year and around 81,000 to 138,000 people die each year because of snake bites.[1] In Africa alone, 435,000 to 580,000 victims[2] suffer snakebite envenoming and South Sudan could be one of the countries with the highest incidence. However, snakebite still receives less attention globally than other Neglected Tropical Diseases (NTDs) and comprehensive programmes and efforts to provide care to snakebite patients are limited.

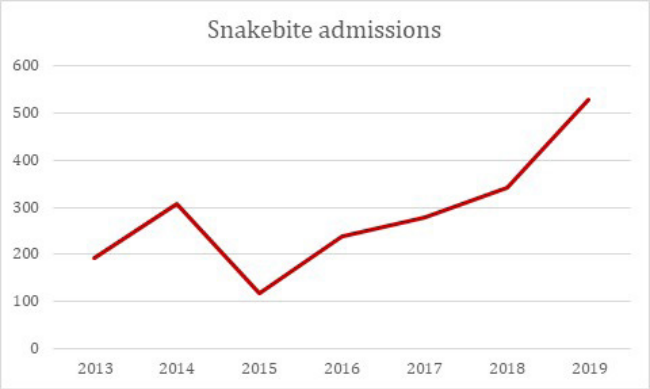

Figure 1. Snakebite admissions

Due to the high number of snakebite admissions, the limited availability of antivenom, and the serious negative outcomes if left untreated, Médecins Sans Frontières (MSF) has been implementing a Snakebite Programme as part of its medical activities at Agok hospital, in the Special Administrative Area of Abyei since 2014.

MSF started nutritional medical activities in 2006 in the Abyei region. However, in 2008, conflict and violence displaced hundreds of thousands of people, including the MSF team, to the far south of the region. MSF started providing nutritional care and expanded activities to inpatient care in the town of Agok. Today, MSF's hospital in Agok is the only secondary health care facility in the region, with a catchment population of some 140,000 people. On average, the hospital provides more than 4000 consultations and hospitalizes over 800 patients per month.

In 2014, the MSF medical team at the hospital received an unexpected high number of snakebite patients (up to 90 in a single month) for which the organization was not fully prepared. This triggered the need to respond to the significant burden of a neglected disease in Agok and surrounding areas. In addition, pharmaceutical company Sanofi Pasteur announced in 2014 that it would stop producing the only recognized safe and efficient polyvalent antivenom, FAV-Afrique. MSF and the South Sudanese Ministry of Health therefore, implemented a study in partnership with Epicentre, MSF's epidemiological research arm, to assess two new antivenoms and to increase access and quality of care for snakebites. Advocacy for better access to snakebite care and antivenom was also carried out nationally and internationally, including towards the WHO.[1-6]

From January 2013 to December 2019, MSF treated 2,005 snakebite patients in Agok, on average 286 per year. Hospital mortality due to snakebite dropped from 3 deaths in 2014 (on arrival), to only 1 in 2019, despite recent doubling of admissions. Indeed in 2019 alone, MSF provided care for 527 snakebite victims, out of which 47% presented with severe envenoming.

Current implementation

Snakebite patients are considered priority cases in the triage area of the Emergency Room (ER). They are transferred to the Intensive Care Unit (ICU) if signs of envenoming are identified, or to the Inpatient Department for 24 hour-observation if no alarming signs are present. Severely envenomed patients are kept in the ICU as long as the antivenom is indicated and receive continuous intensive monitoring to identify and respond to decompensation or shock, swelling, bleeding, neurological disorders, and severe adverse reactions due to the antivenoms, such as allergic or anaphylactic reactions (10% mild, <1% severe).

Surgery can be required in severe cases and is an essential component of the snakebite treatment programme. The hospital surgeons intervene for compartment syndrome (compression of the veins in the muscles due to swelling) or when gangrene is suspected. If needed, fasciotomies are performed, and unfortunately also amputations of toes, fingers, or feet when patients present late with advanced envenoming. At the hospital, snakebite injuries are the fifth leading cause of surgical intervention among all performed surgical interventions. In 2019, 66 procedures among the total 527 snakebite patients represented 9.4% of all surgical interventions.

Figure 2. A MSF nurse changes the dressing of Aluk Manut. (© Fanny Hostettler / MSF)

Figure 3. MSF physiotherapist Ngong Ngong (left) provides physiotherapy to snakebite patients. (© Fanny Hostettler / MSF)

Aluk Manut, aged six, was bitten by a snake on her right leg. Aluk and her mother, Teresa Aluoc Majok, travelled 150 km by public transport from Gogrial to get to the hospital in Agok, South Sudan. Aluk received three doses of antivenom and has had seven surgical interventions. (Figure 2) In figure 3, MSF physiotherapist Ngong Ngong provides physiotherapy to snakebite patients to prevent the total loss of function in their limbs. Sometimes, the severity of the pain means the physiotherapy must be performed under anaesthesia. Here, Awien Maguor, aged 10, was bitten on her arm by a snake while she was sleeping under her mosquito net. She received three doses of antivenom and has had more than ten surgical interventions.

Whole Blood Clotting Test (WBCT20) is the standard coagulation test method, as recommended by the WHO snakebite management guidelines. It can be performed immediately at the bedside with modest resources and has the advantage of giving results in 20 minutes. However, the method also presented some performance issues when utilized in a limited resource context due to implementation challenges.

WBCT20 (sensitivity 94% and specificity 76%)[7] is systematically performed when patients are admitted into the ER, and again 6 and 24 hours after arrival. Clinical features indicating haemotoxicity are paramount to take diagnostic and treatment decisions regardless of confusing test results.

Currently, there are two available antivenoms in the programme. The first, Equitab Plus by ICP (Costa Rica), is used to cover the majority of cytotoxic and haemotoxic envenoming cases according to MSF protocol. It was designed to neutralize the venom of Echis ocellatus, the West African carpet viper and its East African cousin Echis pyramidum, as well as Bitis arietans puff adders' and Naja nigricollis spitting cobras' venoms (the last 2 species are frequent in Agok). The second, SAIMR-Polyvalent, is reserved for the rare cases of neurotoxic envenoming or critically ill patients according to MSF protocol. It is effective against cobras' (Naja), mambas' (Dendroaspis), and some large vipers' (including Bitis arietans frequent in Agok) venoms. These two antivenoms have proven successful in a clinical setting like Agok Hospital, mainly due to the training of medical staff in administering and evaluating the treatment.

Between 2014 and 2016, MSF medical teams simplified the 2010 WHO guideline into a pocket guide for South Sudan. After consulting with the Ministry of Health and receiving authorizations by the Drug and Food Control Authority (DFCA), we introduced a syndromic protocol (Figure 4 and Table 1) and started importing the two previously mentioned antivenoms. By that time, all remaining stocks of the internationally recognized polyvalent antivenom FAV-Afrique (Sanofi) had been used up and the manufacturer had stopped producing it.

Achievements and discussion

MSF has responded to the burden of snakebites, enforcing the supply of antivenom and the cold chain, reviewing and improving algorithms, and strengthening knowledge and skills to better diagnose and manage snakebites. As a result, the delivery of care through a comprehensive programme and adequate health care may be one of MSF's major achievements when tackling one of the most neglected conditions in the world.

The integration of surgical services has proven essential when responding to complicated cases and is one of the main assets of the snakebite programme in Agok. Logistics have also played an important part in the successful implementation of the programme. With the support of national authorities, antivenoms have been procured and imported, thus facilitating the complex supply chain process. Logistics actively maintain a cold chain to avoid ruptures in order to guarantee the availability of a safe antivenom. At the hospital, 24/7 power supply via diesel generators and solar panels has been installed. This shows that it is fundamental to have a multisectoral approach.

Besides clinical interventions, a monitoring study has been implemented since April 2018, in collaboration with the South Sudanese Ministry of Health. It examines the use of Equitab Plus and SAIMR antivenoms, advancing the efforts to generate evidence and to increase access and quality of care for snakebites. The scientific aim of the study, approved by the Ministry of Health and Ethics Committee, is to monitor snakebite patients to describe all clinical symptoms, cure rates, and adverse reactions through regular clinical evaluations of vital signs, swelling size, clotting tests at 0, 6 and 24 hours, and neurological signs. We try to identify snake species by comparing patient descriptions of them with photographs.

So far, the community of Agok is receptive, positively accepting the research implementation and consenting to be enrolled. In part, this is due to the overall good acceptance of the local population towards the hospital during the last 10 years.

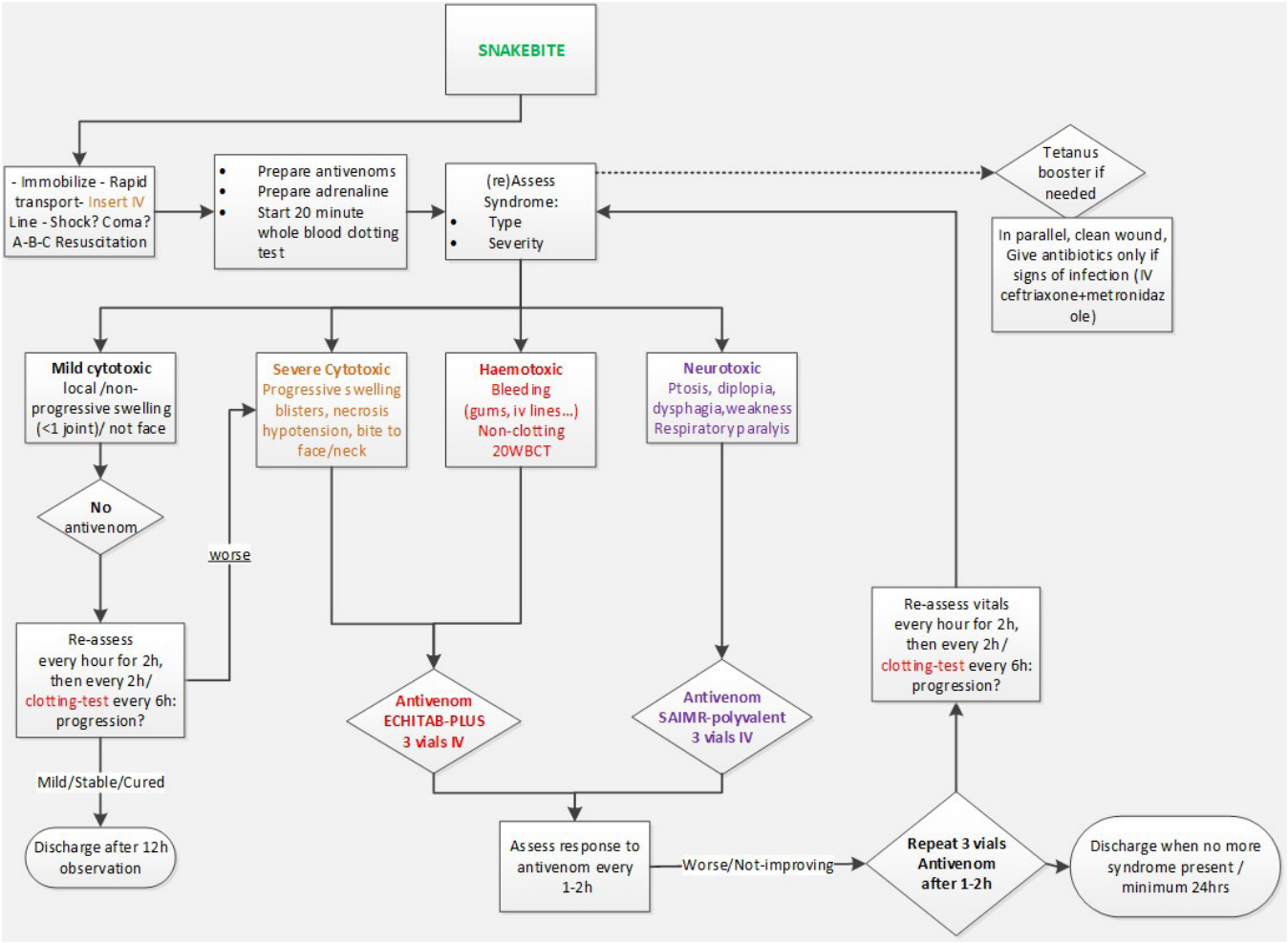

Figure 4. MSF Agok Snakebite Protocol algorithm

Table 1: MSF Agok Snakebite syndromic classification

Syndromes	**Cytotoxic (pain, swelling, shock if severe)**	**Haemotoxic Bleeding, non-clotting** *'Viperid syndrome'*	**Neurotoxic Progressive paralysis** *'Elapid syndrome'*
Species Severity	• **Puff adders** *Bitis arietans* • **Carpet vipers** *Echis spp* • **Spitting cobra** *Naja nigricollis* • Mild: vipers, colubrids	• **Carpet vipers** *Echis* pyramidum • **Puff adders** *Bitis arietans* • Rarely boomslang	• **Egyptian Cobra** *Naja haje*, • **Black Mamba** *Dendroaspis polylepis* & others
Mild >> *No antivenom needed*	Local swelling with no extension beyond 1 joint, Consider antivenom for finger/toe (risk amputation) and face/neck (risk on airways)		
Severe envenoming >> *Antivenom rapidly*	Systemic signs: Hypotension/shock, persistent tachycardia, persistent vomiting/diarrhea, abnormal thoracic pain		
	Rapid swelling Beyond knee/ elbow 4 hours post-bite Half a limb > 15 cm/hour Face/neck.	**Prolonged bleeding** from fang punctures or wounds; or gums/mouth. Severe headache	**Bilateral ptosis** (droopy eyelids), difficult speech. Paraesthesia, excessive sweating, salivation, strange taste, myosis
Severe + life-threatening >> *Antivenom + life-support*	Swelling of whole limb	Positive clotting test (20'WBCT non-clotted)	Weakness, trismus, shortness of breath, respiratory paralysis
	Hypotensive shock. Swelling threatening airway, compartment syndrome, necrosis of limb, amputation.	Spontaneous bleeding or hematomas. Hemorrhagic shock Convulsions (cerebral hematoma)	Bradypnea, respiratory failure, hypoxia - Coma or myocardial infarction.

Challenges and barriers

Agok is a flat land with seasonal swamps. Flooding due to heavy rain in the wet seasons displace snakes from their habitats (holes in the soil) to look for dry and raised land and this exposes people to bites while carrying out different activities such as farming, fetching water, fishing, or even sleeping indoors.

The poverty level and vulnerability of the population also put some people at risk of snake bites. For instance, people cannot afford to buy protective gear such as boots or closed shoes. Rural paths can be dark, making it easy to accidentally tread on a snake. Some traditional house constructions are snake-prone, food storage is not always separated, attracting rodents that in turn attract snakes. Finally, sleeping on the ground without a mosquito net can also increase the risk of being bitten.[8]

Ensuring provision of antivenom is one of the most important challenges, particularly after the production of the "gold-standard" polyvalent FAV-Afrique antivenom was stopped in 2014 by Sanofi Pasteur. The last vial of FAV-Afrique expired in 2016. Since then, Equitab Plus (Costa Rica) and SAIMR (South Africa) antivenoms, also effective,[9] were successfully introduced in MSF's Agok hospital but their extremely high price is a major constraint in ensuring their availability across primary healthcare centres more widely in South Sudan and elsewhere. The price of a vial of Equitab Plus is around 35 USD and SAIMR is around 300 USD per vial. Three vials are needed for a standard treatment, and this dose may be repeated once or twice, depending on severity. The overall cost is therefore out of reach for the vast majority of health facilities and patients.

Another significant challenge is the remoteness of the area and the long time it takes patients to reach the hospital. During the rainy season (July to November), bad roads and lack of transport make timely access to the hospital almost impossible. Delays can increase the risk of complications, long term sequelae, disabilities, and mortality.

Local beliefs and traditions also influence the management of patients. Snakebite victims may delay seeking care due to preference of traditional medicine, causing complications which require additional care.[10] In some instances, patients are reluctant to receive surgical interventions even if strongly needed and recommended. Fasciotomies and amputations are understandably difficult to accept. Counselling and health education are provided to support patients in taking informed decisions. However, sometimes this is not enough and surgical procedures for severe complications are simply refused. It is important to find ways to address this in order to diminish the negative health outcomes of snakebites.

Conclusions and recommendations

The medical and antivenom component of snakebite management is paramount, but a significant number of complications would not be addressed without integrated surgical services. It is therefore, important to gain acceptance of the local population for surgical interventions when required.

The general implementation of the MSF snakebite programme has been successful and keeps improving thanks to standardized treatment protocols, close supervision, strong logistical and pharmaceutical teams overseeing the supply and cold chains, as well as the support from and collaboration with health authorities to facilitate the procurement of the antivenoms.

Polyvalent antivenoms effective in treating envenoming from a broad number of snake species need to be made affordable and accessible to provide health providers, including in low-income settings, with the means to save the lives of snakebite victims.

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