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# Snakebite case management: a cohort study in Northwest Ethiopia, 2012-2020

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## Abstract

Introduction: Timely and appropriate management of snakebites in the tropics is a lifesaver. Many snakebite patients are being bitten in remote rural areas and do not manage to get in due time to healthcare facilities. This study assessed the clinical features and the risk factors associated with treatment outcomes of snakebite patients admitted at two hospitals in the Northwest of Ethiopia.

Methodology: In a retrospective cohort study, routinely collected data from 250 patients' medical charts at University of Gondar Hospital and Metema Hospital, between September 2012 and August 2020, were reviewed.

Results: The median age of the snakebite cases was 24 years (95% CI = 22-26), with 80.8% male patients. At admission 148/250 patients presented in Clinical stage 1 or 2 (local symptoms only) and 73.7% presented more than 12 hours after the bite, 80.2% received antibiotics and 79.0% antivenom. The median duration of hospitalization was 3 days (95% CI = 3-4); 72% of the patients recovered and were discharged, 10.8% died and 0.5% underwent an amputation. On logistic regression analysis, residence in rural areas (AOR = 2.52, 95 % CI = 1.2-5.3), sign of bacterial superinfection on the bite site (AOR = 4.69. 95% CI = 1.4-15.4), clinical stage 3 or 4 with systemic symptoms or toxic signs at admission (AOR = 4.84, 95% CI = 1.3-18.0) and no treatment with antivenoms (AOR = 6.65, 95% CI = 1.6-27.7) were associated with bad outcome (death, amputation and/or referred/ went against medical advice).

Conclusions: Timely presentation at early clinical stage, appropriate clinical management and availability of antivenoms are cornerstones to reduce snakebite morbidity and mortality.

**Key words:** Neglected tropical diseases; management of snakebite; sub-Saharan Africa; operational research; SORT IT.

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## Introduction

Snakebite envenoming is a potentially life-threatening disease, listed by the World Health Organization (WHO) as one of the high public health priorities among neglected tropical diseases (NTDs) [1]. In rural areas of low-and middle-income countries (LMIC), especially among the poorest population groups, snakebites are causing a huge burden in terms of morbidity and mortality [2]. Worldwide, every year an estimated 5.4 million people are bitten by snakes, causing nearly 400,000 amputations and 81,000–138,000 deaths. The majority of fatalities occur in Asia (14,000) followed by sub-Saharan Africa (estimated to range between 3,500–32,100 deaths/year) [1,3].

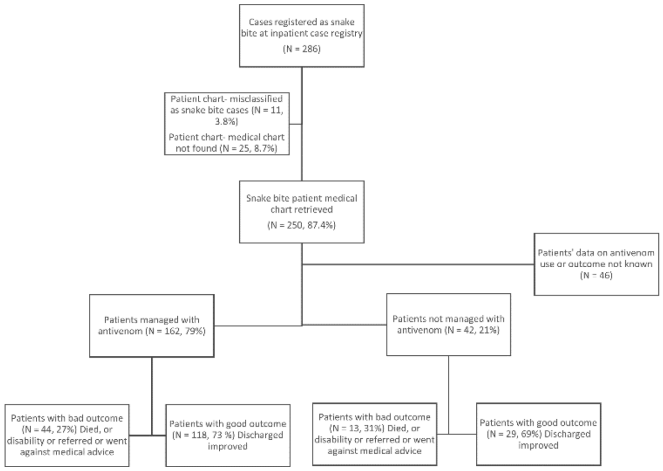
Snakebite envenomation is a medical emergency which may lead to multi organ failure manifested by hemorrhage, coagulation defect, renal and cardiac failure, neuromuscular paralysis and tissue necrosis which, without effective management, leads to death [4,5]. In rural settings, snakebite patients, living far from health centers, are likely to use traditional "first aid techniques" (local incision, suction, traditional herbs, tight tourniquets, wound washing, among other interventions) before seeking medical care at the nearest health facility [6]. Most deaths and serious consequences from snakebites, such as limb amputation, could be prevented if safe and effective antivenoms would become widely available in peripheral health facilities, close to where the most affected people live or work [1].

The exact burden of snakebites in Ethiopia is unknown and the health problem is potentially

underestimated because reporting is not compulsory. A PubMed and Google scholar search showed few reports in Ethiopia on snakebites: four cases in Aysha refugee camp in the year 1999 [7], two cases reported from Addis Ababa University in the year 2018 [8], one case series reported on case presentation and clinical management [9] and one national survey [10]. The latter conducted in 2011-12, reported 949 snakebites over a 10-month period in 76 health facilities in Ethiopia, showing that snakebites were observed in many different regions of the country and that patients often did not seek medical care. The reasons put forward for this were: lack of sufficient knowledge and experience with appropriate treatment, lack of antivenom at government dispensaries, and long distance between the location where the snakebite occurred and the health facility [10]. The mentioned snakebite case series was a study of 27 cases followed between September 2013 and August 2014 at the University of Gondar Hospital (UoGH) [9]. Twenty-five patients presented ≥ 12 hours after the snakebite with most of them already showing bleeding disorders. The reported case fatality rate was 14.8% [9].

There is an urgent need to have more data and information on the burden, especially on morbidity and mortality, of this health problem in Ethiopia [1,7]. This evidence would facilitate the estimation of need for antivenom and contribute towards successful implementation of a prevention and control strategy as recommended by WHO [2], in line with the WHO NTD roadmap 2021-2030 while contributing to WHO Snakebite Information and Data Platform [11]. This study will assess the risk factors associated with the treatment outcomes of snakebite patients through the analysis of routinely collected data at two hospitals in Northwest Ethiopia, UoGH and Metema Hospital.

**Figure 1.** Flowchart of the retrospective cohort study.




## Methodology

*Study Design and period*

This is a retrospective cohort study, using routinely collected data from patients' medical charts at UoGH and Metema Hospital, between September 2012 and August 2020.

*General Setting*

Ethiopia is located in east Africa and is bordered by six countries. The country's estimated population in 2016 was 102 million. The health coverage for Ethiopia is 39%, which is one of the lowest records in the world [12]. Ethiopia is a federal state with nine regional states and two special administrations. Ethiopia has the third highest number of NTDs cases in Africa, harboring 16 of the 20 NTDs on the WHO list. Gondar is located 735 km from the capital Addis Ababa and is 200-300 km from the border areas with Sudan.

*Specific settings*

The study was conducted at UoGH and Metema Hospital, respectively a tertiary and primary hospital in Northwest Ethiopia. The UoGH is located in Gondar town (North Gondar, Amhara region, Ethiopia) which is 175 km from Bahir Dar, the capital city of the region. The hospital provides outpatient and inpatient health care, together with outreach health services for about 5 million population in Amhara Regional State.

The university hospital has different departments. The snakebite cases are managed at the emergency unit of internal medicine department with some at pediatrics department and referred to other departments in case of complications.

Metema primary care hospital is located in North Gondar, on the border of Sudan, 897 km Northwest of Addis Ababa and 197 km from Gondar town. The hospital is the only primary hospital in the community which provides inpatient and outpatient services for more than 5,581 inhabitants living in the area. Both hospitals are located near low altitude areas, with big sesame and cotton farms, characterized with an influx of about a quarter million people for seasonal work in the harvesting and farming period [13]. This region is known for having a high burden of snakebites.

*Study population and period*

All individuals presenting to the two hospitals with a snakebite complaint between September 2012 to August 2020 were included in this study (Figure 1). At both hospitals, patients were managed with polyvalent antivenom if their 20 minutes bedside clotting test is prolonged. Antivenom is repeated every six hours till

the bedside clotting test got normal. Patients were followed for antivenom reaction. Complete blood count, liver and renal function tests, and coagulation tests were determined at admission.

*Data collection, sources of data and statistical analysis*

Data variables included socio-demographic information (age, gender, residence, occupation), clinical symptoms and signs (place and date of exposure to the snake, clinical stage, time between bite and presentation at hospital, traditional medication applied before arrival at the hospital), laboratory tests (Complete Blood Count, Liver and Renal Function Test, Bedside clotting test) and type of treatment and treatment outcome (antivenom use, time between presentation and antivenom administration, reaction to treatment, duration of hospitalization, tetanus antitoxin (TAT) administration, antibiotic administration, death, disability, cure). Good outcome was defined as patients discharged improved and bad outcome as patients who got amputated or has permanent disability from the snakebite, died or referred to other hospital for better management or went against medical advice. Clinically, severity was assessed as Stage 1 if patient has fang marks ("dry" bite) due to snakebite; Stage 2, with local findings only (e.g., pain, ecchymosis, non-progressive swelling); Stage 3, with swelling that is clearly progressing, systemic symptoms or signs, and/or laboratory abnormalities; Stage 4, with neurologic dysfunction, respiratory distress, and/or cardiovascular instability/shock. Bedside clotting test is considered as prolonged if whole blood does not clot after 20 minutes of draw. The classification 'no antivenom use', is irrespective of the reason for not receiving antivenom (not clinically indicated, no antivenom available or not accepting antivenom treatment).

Data on patients presenting to both hospitals with a diagnosis of snakebite were retrieved from the paper medical charts kept at their respective card room. We used a Microsoft XL structured data collection sheet for the data entry and EpiData (version 2.2.3.187, EpiData Association, Odense, Denmark) and STATA IC 10.0 for Windows (Statacorp, Texas, USA) for the analysis. Research finding are presented using descriptive statistics. A bivariate analysis was performed on the outcome and all the independent variables (as stated above). Odds Ratios (OR) were calculated, together with its 95% confidence Interval (CI). A multivariable logistic regression was performed to identify risk factors, giving adjusted odds ratios (AORs), including the independent variables showing a significant association in the bivariate analysis.

*Ethics approval*

Permission for using the routine data from paper medical charts was obtained from the University of Gondar, Institutional Review Board. Permissions to collect data were granted from the north Gondar health

**Table 1.** Socio-demographic characteristics of snakebite patients treated at two hospitals in Northwest Ethiopia, 2012-2020.

| Characteristics | N (%) | 95% CI |
|---|---|---|
| **Age N = 249** | | |
| < 15 | 38 (15.3) | 10.8-19.8 |
| 15-45 | 183 (73.5) | 68.0-79.0 |
| > 45 | 28 (11.2) | 7.3-15.2 |
| **Gender N = 250** | | |
| Male | 202 (80.8) | 75.9-85.7 |
| Female | 48 (19.2) | 14.3-24.1 |
| **Residence N = 243** | | |
| Urban | 125 (51.4) | 45.1-57.8 |
| Rural | 118 (48.6) | 42.2-54.9 |
| **Occupation N = 166** | | |
| Farmer | 92 (55.4) | 47.8-63.1 |
| Day labourer | 33 (19.9) | 13.7-26.0 |
| Student | 19 (11.4) | 6.6-16.3 |
| Others | 22 (13.3) | 8.0-18.5 |

**Table 2.** Clinical features of snakebite patients treated at two hospitals in Northwest Ethiopia, 2012-2020 (N = 206, unless otherwise stated).

| Feature | N (%) | 95% CI |
|---|---|---|
| **Place of snakebite exposure N = 183** | | |
| Field | 141 (77.0) | 70.9-83.2 |
| Home | 42 (23.0) | 16.8-29.1 |
| **Time of snakebite N = 180** | | |
| Day | 148 (82.2) | 76.6-87.9 |
| Night | 32 (17.8) | 12.1-23.4 |
| **Time from snakebite to hospital N = 205** | | |
| < 12 hours | 54 (26.3) | 20.8-32.8 |
| >12 hours | 151 (73.7) | 67.2-79.2 |
| **Site of snakebite** | | |
| Upper extremity | 30 (14.6) | 10.4-20.0 |
| Lower extremity | 175 (85.0) | 79.4-89.2 |
| Neck | 1 (0.5) | 0.1-2.7 |
| Presence of fever | 93 (45.1) | 38.3-52.0 |
| Presence of Swelling | 134 (65.0) | 58.5-71.6 |
| **Clinical stage N = 160** | | |
| Stage 1 | 44 (27.5) | 20.5-34.5 |
| Stage 2 | 104 (65.0) | 57.5-72.5 |
| Stage 3 | 8 (5.0) | 1.6-8.4 |
| Stage 4 | 4 (2.5) | 0.5-4.9 |
| **Sign of bacterial superinfection N = 207** | 130 (62.8) | 56.2-69.4 |
| Tie / tourniquet applied | 33 (16.0) | 11.0-21.1 |
| Cultural medication used | 14 (6.8) | 2.7-10.1 |
| Presence of Gangrene N = 207 | 3 (1.4) | 0-2.8 |
| Presence of Bleeding N = 207 | 173 (83.6) | |
| **Site of bleeding** | | |
| Wound site | 154 (89.0) | 83.5-92.9 |
| Epistaxis | 12 (6.9) | 4.0-11.7 |
| Petechial rash | 3 (1.7) | 0.6-5.0 |
| Gum bleeding | 1 (0.6) | 0.1-3.2 |
| Gastrointestinal bleeding | 3 (1.7) | 0.6-5.0 |

bureau and from each hospital administrations. Ethics approval was obtained as well from the Union Ethics Advisory Group of the Center for Operational Research at the International Union against Tuberculosis and Lung Disease, Paris, France.

## Results

In this retrospective cohort study, 250 snakebite patients treated at UoGH and Metema Hospital were included. Their median age was 24 years (95% CI = 22-26, IQR = 18-30 years) and majority, 80.8% were male (Table 1).

The season with highest number of snakebite cases was from September to November (Figure 2). The field was the most frequent location of snakebite (77.0%). 82.2% of snakebites occurred during daytime (Table 2).

When patients presented to the hospital, 148 of them were still in the first or second clinical stage, but 62.8% had already a sign of bacterial superinfection. In 93.2% of the cases, no tie or torniquet was applied. Gangrene was only recorded in 3 patients. Wound site bleeding was reported in 89% of the patients and 73.7% presented to the hospital more than 12 hours after the bite (Table 2). None of the patients in this cohort had neurotoxic signs or symptoms.

In this cohort, for patients with laboratory testing done, anemia was present in 52.1%, while thrombocytopenia and leukocytosis were found in only 25.9% and 32.6% respectively. Bedside clotting test was prolonged in 19.5% of the patients (Table 3).

Out of 207 snakebite patients 166 (80.2%) received antibiotics. Tetanus antitoxin was given to 149 (73.0%). Out of 162 patients (79.0%) who received antivenom, 6 (3.7%) of them showed reaction to the antivenom.

The median time between admission and antivenom administration was 24 hours (IQR = 16-72) with 99.4%

**Table 3.** Laboratory features of snakebite patients admitted at two hospitals in Northwest Ethiopia, 2012-2020.

| Test name | Median (IQR) | N (%) | 95% CI |
|---|---|---|---|
| WBC count ($10^3$cells/µL) (*) N = 95 | 7.9 (6.0-11.5) | | |
| Leukopenia | | 2 (2.1) | 0.6-7.4 |
| Normal range | | 62 (65.3) | 55.3-74.1 |
| Leukocytosis | | 31 (32.6) | 24.0-42.6 |
| Hemoglobin (g/dL) N = 94 | 12.7 (9.5-14.4) | | |
| Anemia (¶) | | 49 (52.1) | 42.1-61.9 |
| No Anemia | | 45 (47.9) | 38.1-57.9 |
| Platelet count ($10^9$ cells/µL) N = 89 | 190 (141.5-359.0) | | |
| No thrombocytopenia (#) | | 66 (74.2) | 64.2-82.1 |
| Mild thrombocytopenia | | 16 (18.0) | 11.4-27.2 |
| Moderate thrombocytopenia | | 3 (3.4) | 1.2-9.4 |
| Severe thrombocytopenia | | 4 (4.5) | 1.8-11.0 |
| Liver function test [a] | | | |
| Aspartate aminotransferase (U/L) N = 13 | 35.6 (25.0-131.0) | | |
| Alanine amino transferase (U/L) N = 14 | 32.3 (26.8-46.2) | | |
| Renal function test | | | |
| Creatinine [b] (mg/dL) N = 22 | 0.86 (0.62-0.92) | | |
| Normal | | 20 (90.9) | 72.2-97.5 |
| Elevated | | 2 (9.1) | 2.5-27.8 |
| Coagulation test [c] | | | |
| Prothrombin time (sec) N = 33 | 15.9 (13.0-21.1) | | |
| Activated Partial Thrombin Time (Sec) N = 33 | 34.3 (26.2-40.5) | | |
| International Normal Ratio N = 32 | 1.32 (1.0-1.6) | | |
| Bedside clotting test N = 87 | | | |
| Prolonged | | 17 (19.5) | 12.6-29.1 |
| Not prolonged | | 70 (80.5) | 70.9-87.4 |
| Serum sodium level (mmol/dL) N = 14 [d] | 139 (137.0-143.0) | | |
| Hyponatremia | | 2 (14.3) | 4.0-39.9 |
| Eunatremia | | 10 (71.4) | 45.4-88.3 |
| Hypernatremia | | 2 (14.3) | 4.0-39.9 |
| Serum potassium level (mmol/dL) N = 14 [e] | 4.0 (3.8-4.3) | | |
| Hypokalemia | | 2 (14.3) | 60.1-96.0 |
| Eukalemia/ normal | | 12 (85.7) | 4.0-39.9 |

IQR: inter quartile range, WBC: white blood cell, Hgb: hemoglobin; (*) Leukopenia WBC count < 4,000, Leukocytosis WBC count > 11,000; (¶) Anemia Hgb level < 12mg/dL for female and < 13mg/dL; (#) Thrombocytopenia, Platelet count 100-150: Mild, 50-100: Moderate, < 50: Sever; [a] Normal value for Aspartate aminotransferase is < 37 U/L and alanine aminotransferase is <42 U/L; [b] Creatinine above 1.1 mg/dL for both sex, is considered elevated; [c] normal range for prothrombin time is 12.7-14.0 sec and for activated partial thrombin time is 60 to 80 second; [d] Sodium level < 135, Hyponatremia, Eunatremia, sodium 135-145, hypernatremia, > 145; [e] Potassium level < 3.5 hypokalemia, 3.5-5.5 , eukalemia, > 5.5 hyperkalemia.

(161) of the patients receiving antivenom within the first hour of admission. The median duration of hospitalization was 3 days (95% CI = 3-4); 72.1% (147) of the patients had a positive evolution and were discharged while 22 (10.8%) died, 1 (0.5%) had amputation and 34 (16.7%) were referred to another hospital for better management or were discharged against medical advice (Table 4).

The logistic regression analysis (on 158 patients with full information on the selected variables) revealed that factors associated with bad outcome were residence in rural areas (AOR = 2.52, 95 % CI = 1.2-5.3), sign of bacterial superinfection on the bite site (AOR = 4.69. 95% CI = 1.4-15.4), clinical stage 3 or 4 at presentation, (AOR = 4.84, 95% CI = 1.3-18.0) and no treatment with antivenom (AOR = 6.65, 95% CI = 1.6-27.7) (Table 5).

## Discussion

In our study, we found that snakebite affects mostly male adults between the age group of 15 to 44 years old. 57 (22.9%) of the patients in our study are less than 18 years old, in contrast to a study in Nigeria, where only 13 paediatric cases were seen over a seven-year period [14]. In the majority of cases, snakebites occurred in the field during day time on the lower extremities. This is similar to studies done in other settings [9,10,15-17].

In this cohort, almost three-quarter of the patients presented to the hospital late (> 12 hours) after the bite occurred. Commonly patients had fever, swelling, sign of bacterial super infection and bite site bleeding. More than half of the patients presented with a clinical Stage 2 implying local findings only such as pain, ecchymosis and non-progressive swelling. Unlike other studies, only a small percentage of patients applied tie/ torniquet or use cultural medication in our study. This may be due to the fact that patients who seek traditional medication may stay in the community and are not attending hospitals [18] but still it shows a high number of patients not following first aid treatments recommended by WHO [5]. Of the patients who had complete blood count determination, anemia was found in half of them while leukocytosis and thrombocytopenia were found only in one third of the cases. In our study, in addition to the normal record of coagulation laboratory tests (prothrombin time, activated partial thrombin time and international normal ratio), the 20-minute bedside clotting test was prolonged only for 17 (19.5%, 95% CI = 12.6-29.1) of the patients, this is lower than the 63.7% in patients seen in eastern Ethiopia [15]. Lack of continuous availability of reagents to determine coagulations tests in our setup may explain why only a small portion of the patients had these tests done.

This is a retrospective cohort study on the basis of patient records routinely collected in a hospital setting. Snakebites are frequently occurring in the study area, and hence 250 patients were included in this study. The relative weakness of working with routine data is the missing of some information, such as laboratory tests, which could be due to absence of clinical indication, no reporting, or no availability of tests. Another limitation is that routine information is less standardised than experimental research data, although supervision and revision of data was repeatedly done by the first author, who was the main medical doctor treating these patients over the years.

**Table 4.** Treatment and treatment outcome of snakebite patients admitted at two hospitals in Northwest Ethiopia, 2012-2020.

| Feature | N (%) | 95% CI |
|---|---|---|
| Antibiotic given N = 207 | 166 (80.2) | 74.7-85.1 |
| Tetanus antitoxin given N = 204 | 149 (73.0) | 66.9-79.2 |
| Antivenom given N = 205 | 162 (79.0) | 73.4-84.6 |
| **Time between Antivenom and presentation at the hospital (hours) N = 162** | | |
| < 1 | 1(0.6) | 0.1-3.4 |
| > 1 | 161 (99.4) | 96.6-99.9 |
| No of vials (Median (IQR)) | 2 (1-3) | |
| Reaction to antivenom | 6 (3.7) | 1.7-7.9 |
| Duration of hospitalization (in days) median (IQR) N = 204 | 3 (3-4) | |
| **Patient outcome N = 204** | | |
| Discharged and improved | 147 (72.1) | 65.8-78.3 |
| Died | 22 (10.8) | 6.5-15.1 |
| Disability/amputated | 1 (0.5) | 0-1.5 |
| Referred/ went against medical advice | 34 (16.7) | 11.5-21.8 |

IQR: inter quartile range.

**Figure 2.** Monthly snakebite cases at University of Gondar and Metema Hospital, Ethiopia, 2012-2020.

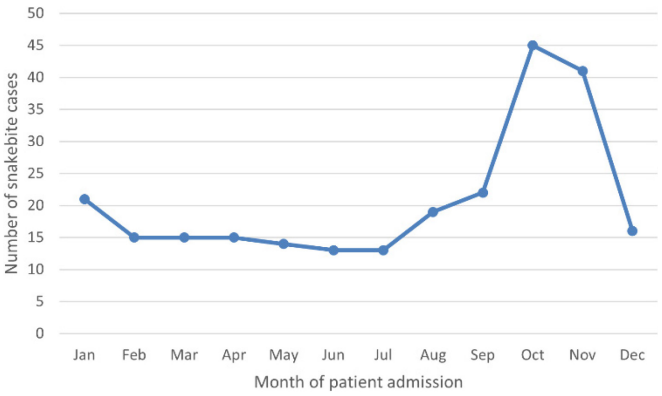


**Table 5.** Characteristics associated with treatment outcome among snakebite patients treated in two hospitals in Northwest Ethiopia, 2012-2020.

| Characteristics | Number | Bad outcome, n (%) | OR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|
| **Age** | | | | |
| < 15 | 36 | 12 (33.0) | 1 | |
| 15-45 | 151 | 39 (26.0) | 1.44 (0.7-3.1) | |
| > 45 | 17 | 6 (35.0) | 0.92 (0.3- 3.1) | |
| **Gender** | | | | |
| Male | 165 | 51 (31.0) | 2.46 (1.0-6.2) | |
| Female | 39 | 6 (15.0) | 1 | |
| **Residence** | | | | |
| Urban | 103 | 21 (20.0) | 1 | 1 |
| Rural | 101 | 36 (36.0) | 2.16 (1.2- 4.1) | 2.52 (1.2-5.3) |
| **Clinical stage** | | | | |
| Stage 1 and 2 | 146 | 39 (27.0) | 1 | 1 |
| Stage 3 and 4 | 12 | 7 (58.0) | 3.8 (1.2-12.8) | 4.84 (1.3-18.0) |
| **Antivenom given** | | | | |
| Yes | 162 | 44 (27.0) | 1 | 1 |
| No | 42 | 13 (31.0) | 1.2 (0.6-2.5) | 6.65 (1.6-27.7) |
| **Sign of bacterial superinfection** | | | | |
| Yes | 128 | 43 (34.0) | 2.2 (1.1- 4.5) | 4.69 (1.4-15.4) |
| No | 76 | 14 (18.0) | 1 | 1 |
| **Tie/ Tourniquet application** | | | | |
| Yes | 32 | 12 (38.0) | 1 | |
| No | 171 | 45 (26.0) | 0.6 (0.3 -1.3) | |
| **Cultural medication** | | | | |
| Yes | 14 | 5 (36.0) | 1 | |
| No | 189 | 52 (28.0) | 0.7 (0.2- 2.1) | |
| **Gangrene** | | | | |
| Yes | 3 | 2 (67.0) | 1 | |
| No | 201 | 55 (27.0) | 0.19 (0.0- 2.1) | |
| **Time from snakebite to hospital** | | | | |
| < 12 hours | 53 | 12 (23.0) | 1 | |
| > 12 hours | 149 | 43 (29.0) | 1.4 (0.7-2.9) | |
| **WBC (Median) (*)** | | | | |
| No leukocytosis | 64 | 16 (25.0) | 1.39 (0.5-4.0) | |
| Leukocytosis | 31 | 6 (19.0) | 1 | |
| **Hgb (Median) (¶)** | | | | |
| Anemia | 49 | 16 (33.0) | 2.2 (0.9- 5.9) | |
| No Anemia | 45 | 8 (18.0) | 1 | |
| **Platelet counts** | | | | |
| Normal | 66 | 14 (21.0) | 1 | |
| Thrombocytopenia | 23 | 8 (35.0) | 2.0 (0.7 -5.6) | |
| **Creatinine** | | | | |
| Normal | 20 | 5 (25.0) | 1 | |
| Elevated | 2 | 1 (50.0) | 3.0 (0.2- 57.4) | |
| **Prothrombin time** | | | | |
| Prolonged | 23 | 4 (17.0) | n.a. | |
| Not Prolonged | 10 | 0 (0.0) | n.a. | |
| **Activated partial thromboplastin time** | | | | |
| Prolonged | 32 | 4(13.0) | n.a. | |
| Not Prolonged | 1 | 0 (0.0) | n.a. | |
| **International Normalized Ratio** | | | | |
| Prolonged | 10 | 3 (30.0) | 8.14 (0.7-91.9) | |
| Not Prolonged | 20 | 1(5.0) | 1 | |
| **Bedside clotting test** | | | | |
| Prolonged | 17 | 4 (24.0) | 1 | |
| Not prolonged | 70 | 17 (2.0) | 1.0 (0.3-3.6) | |
| **Antibiotics** | | | | |
| Yes | 164 | 47 (29.0) | 1.2 (0.6-2.7) | |
| No | 40 | 10 (25.0) | 1 | |
| **Tetanus antitoxin given** | | | | |
| Yes | 149 | 39 (26.0) | 1 | |
| No | 55 | 18 (33.0) | 1.4 (0.7 -2.7) | |

IQR: inter quartile range, WBC: white blood cell, Hgb: hemoglobin, OR: odds ratio, AOR: adjusted odds ratio; (*) Leukopenia WBC count < 4,000, Leukocytosis WBC count > 11,000; (¶) Anemia Hgb level < 13mg/dL; (#) Thrombocytopenia, Platelet count 100-150: Mild, 50-100: Moderate, < 50: Severe.

In this cohort, antibiotics, tetanus antitoxin and one or more vials of antivenom were given for 80.2%, 73% and 79% respectively. 10.8% (22) patients died of snakebite complications, this is less than the cases reported previously from UoGH and Nigeria but higher than the study reported from Dilchora hospital, Ethiopia, South Africa and India [9,15,19-21].

Although, in our study, we did not have details on treatment for antivenom reactions, the frequency that we observe of n = 6/205 (3.7%, 95% CI = 1.7-7.9) is comparable to findings from India (N = 4, 5.5%) [21].

Residence in rural areas and an advanced clinical stage were associated with bad outcomes. This may be due to the distance from the residence to the health facility which may delay timely interventions and development of severe disease. Antivenoms are the cornerstone of snakebite management, but they have to be given in a timely manner. For patients who has indication for antivenom, which is prolonged bedside clotting test in our setup, antivenom has to be given to the earliest. The antivenoms used at the study sites were Snake Venom Antiserum Polyvalent injection, Vins Bioproducts Ltd, which are active against the most common snake species in the area, Echis pyramidum, Bitis arientans [22]. The median time between antivenom administration and hospital admission was 24 hours (IQR = 16-72). Medicins Sans Frontières (MSF) recently published data from northwest Ethiopia showing a median duration between admission and antivenom administration to be 8.8 hours, IQR = 0.0–24.4 hours but similar to our finding it was not associated with bad outcomes of patients [22]. In a study done in India, patients who received antivenom within six hours had less adverse outcomes than those who received it after six hours of a bite [23]. Unavailability, inadequate administration, unaffordability, and reaction to antivenom are known to be risk factors for bad outcome of snakebite management. In 2008, similar to our study done in Brazil, no use of antivenom was associated with having bad outcome [24] and antivenom administration had protective effect on mortality [25]. Although, diagnosis of bacterial super infection in the presence of systemic inflammation due to the bite is difficult, we found it in 62.8% (95% CI = 56.2-69.4) of the patients. We observed that these patients have more than 4 times the risk of having a bad outcome (AOR = 4.69, 95% CI = 1.4-15.4), which may strengthen the use of empiric antibiotic treatment in our settings. The retrospective nature of this study does not allow data to be collected on antibiotic choice, response to antibiotic treatment and associated resistance with empiric use, which needs further investigation.

The burden of snakebite in Ethiopia and neighbouring countries are estimated to be high and the available data are possibly underreporting and underestimating the real burden. The Ethiopian national epidemiological survey reports 949 cases within a 10 month period [10]. In areas where MSF is operating, the routinely collected data show that annual snakebite cases in Ethiopia and South Sudan has increased from a few hundreds to more than a thousand [26]. Similarly, in Kenya snakebite was reported in 13.1% of the respondents in a community while in Sudan 12623 snakebite cases were seen annually [27]. Interrupted supply of antivenoms, unaffordability of the antivenom, going to traditional healers, humanitarian crisis and the study being a hospital-based may contribute as factors for the underestimation of snakebite burden.

Our study provides information for estimating the burden of snakebites in this region of Ethiopia and on global level, but more importantly on the management of snakebites. The recognition of factors associated with bad outcome, will guide the clinicians to identify patients who need to be treated with priority and also hospital administration to provide sufficient doses of antivenoms and other supportive medical and laboratory commodities. A study in the communities, evaluating snakebite morbidity, severity and mortality would be a logical complement to provide a holistic view on the burden and impact of this disease on the population's health.

## Conclusions

The case fatality rate associated with snakebite is high. Timely presentation to the hospital at early clinical stage, appropriate clinical management, and availability of antivenoms are cornerstones to reduce snakebite morbidity and mortality. Further collaboration among stakeholders (community, health and agriculture sectors, professional associations, and civil society) must be established and strengthened to improve management of snakebite patients at different levels.

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