

1 Evaluation of management of snake bites in a teaching hospital in Northern Ghana- a
2 retrospective descriptive study

3

4

5 Abdul-Subulr Yakubu,^{1*} Alhassan Abdul-Mumin,^{2,3} Odalys Rivera^{1,3}

6

7 ¹ Department of Internal Medicine, Tamale Teaching Hospital, Box TL 16 Tamale, Ghana

8 ²Department of Paediatrics and Child Health, Tamale Teaching Hospital, Box TL 16 Tamale,
 9 Ghana

10 ³University for Development Studies, School of Medicine and Health Sciences, Tamale, Ghana

11

12

13

14 *Corresponding author

15 Email: subulr87@gmail.com

16

17

18

ABSTRACT

BACKGROUND: Snakebite is a public health problem afflicting mainly rural farmers. We seek to examine the profile and management of snakebite cases presenting to the Tamale Teaching Hospital of Ghana over a 30-month period.

METHODS: One hundred and ninety-two cases of snakebites presenting to the Tamale Teaching Hospital over a 30-month period from January 2016 to June 2018 were retrospectively analyzed. Information about the clinical manifestation of the snakebites, treatment instituted as well as the outcome was extracted from patient folders for the analysis.

RESULTS: Out of the 192 cases of snakebite, 131 (68.2%) occurred in males. The mean age of the victims was 26.5 years. The major patterns of envenomation were coagulopathy (84.9%) and local swelling/pain (82.8%). The causative snake species was identified in only 11.5% of cases, all of which were vipers. Antivenom was administered in 94.8% of the victims and the average amount administered was 84.64 milliliters (approximately 8 vials). Reaction to antivenoms was observed in 13.5% of cases, comprising mostly minor reactions. Antibiotics were utilized in 99.5% of cases with more than half receiving more than one type of antibiotic. Steroids use was common (62%) whilst 22.9% received antifibrinolytics despite the absence of evidence supporting their use in snakebite.

CONCLUSION: Snakebite is an occupational health hazard of mainly rural farmers. The unwarranted use of non-beneficial medications is still rife. In addition to ensuring the continuous availability of effective antivenoms, there is the need for the development and adherence to protocols that take into consideration the prevailing local conditions.

Key words: Snakebite; Ghana; Antivenom; Envenomation; Carpet viper

AUTHOR SUMMARY

Snakebite affects mainly rural farmers and is a disease of poverty. Unreliable epidemiological data in developing countries like Ghana makes ascertaining the true extent of snakebite difficult. We have examined the presentation and clinical management of snakebite cases presenting to the Tamale Teaching Hospital of Ghana which serves a mainly rural population. The Carpet Viper, which produces a syndrome of local swelling and bleeding, is implicated in most snakebites in this region. A variety of non-evidenced-based interventions are employed by medical personnel in managing snakebite victims underscoring the need to have written contextually appropriate protocols for snakebite management. Public education is also needed to minimize the delays in seeking healthcare following a snakebite whilst efforts at ensuring the continuous availability of effective antivenoms must be intensified.

INTRODUCTION

Snakebite is a life-threatening medical emergency predominantly affecting rural farmers [1] which has been listed amongst the World Health Organization's (WHO) Neglected Tropical Diseases (NTD) [2]. It remains an under-addressed public health problem in developing countries like Ghana [3,4].

The exact extent of the menace of snakebite is difficult to ascertain due to lack of reliable epidemiological data in most developing countries like Ghana. This is compounded by the fact that most bites are managed at home or by traditional healers [1,5,6]. Globally, it is estimated that the incidence of envenomation is in excess of five million a year, with about 100 000 of these cases developing severe sequelae [6,7]. Nigeria records 174 snake bites/100 000 population/year [8] whilst Northern Ghana has an estimated 86 envenomings and 24 deaths/100 000/year caused mainly by *Echis ocellatus* [1].

The carpet or saw-scaled viper (*Echis ocellatus*) is by far the most important cause of fatal or debilitating snake bite in sub-Saharan Africa, north of the Equator [1,9–13]. It is responsible for 90% of bites in Nigeria [8]. It causes a clinical syndrome with painful local swelling, tissue damage and necrosis and coagulopathy with potentially fatal haemorrhage [14]. Bites may be complicated by disfigurement, mutilation, tissue destruction, amputation, blindness, disability, and psychological consequences [15]. The systemic effects of this venom are however readily reversible by specific antivenoms; spontaneous systemic bleeding stopping, in the majority of cases, within 2 hours and coagulopathy corrected within 6 hours of administration of a single dose of a potent specific antivenom [13,16,17]. The other important causes of serious

81 envenomation in sub-Saharan Africa are the black-necked spitting cobra (*Naja nigricollis*) and
82 puff adder (*Bitis arietans*) [13,15].

83 There is a wide variation in the management principles employed by healthcare workers in the
84 management of snakebites in Ghana. The use of locally developed protocols that are adaptable to
85 the prevailing healthcare structure and capabilities should be encouraged [18]. Staff training,
86 adherence to written protocols and patient education have been shown to significantly improve
87 outcomes in snakebite cases in a rural hospital (Mathias Hospital) in Ghana [19].

88 We seek to examine the management choices and eventual outcome of snakebite cases
89 presenting to the Tamale Teaching Hospital (TTH) in the Northern Region of Ghana over a 30-
90 month period from January 2016 to June 2018.

91

92 **METHODS**

93 **STUDY AREA**

94 The Northern Region of Ghana has a population of 2,479,461 (of which 50.4% are female) and
95 occupies an area of about 70,384 square kilometres. A large proportion of its economically
96 active group are engaged in agriculture[20] and the population is predominantly rural (69.7%).
97 The TTH receives referrals from all hospitals in the Northern, Upper East and Upper West
98 Regions of Ghana.

99 **STUDY DESIGN**

100 This is a retrospective descriptive study which focuses on the management of all confirmed
101 snakebite cases presenting to the TTH over a 30-month period from January 2016 to June 2018.

102 DATA COLLECTION TECHNIQUE

103 The case records of patients presenting with snakebite through the Emergency or Out-patient
 104 departments of the Medical and Paediatrics departments of TTH were retrieved for the period
 105 January 2016 to June 2018. Demographic information as well as treatment administered,
 106 complications arising, laboratory indices and outcome was extracted from the folders and
 107 reviewed. The opinion of the treating physician was taken with regards to identification of the
 108 type of snake responsible for the bite. Cases in which the cause of the bite was in doubt by the
 109 treating physician were excluded. Stringent measures were taken to ensure anonymity of the
 110 patients. Information obtained did not identify individuals by name and only authorized
 111 personnel were granted access to patient folders. The Research and Development Department of
 112 the TTH granted approval for the study (with permission number TTH/R&D/SR/13) which was
 113 exempted from full institutional ethical review.

114 DATA ANALYSIS

115 The Statistical Package for Social Sciences (SPSS) version 20 was used for data entry and
 116 analysis. Descriptive statistics was used, and results presented as means $\pm$ standard deviation for
 117 continuous variables and percentages for discrete variables.

118

119 RESULTS

120 Clinical Profile

121 One hundred and ninety-two snake bite cases were recorded over the 30-month period. 131 of
 122 these were male (68.2%) and 61(31.8%) female. The ages of the victims ranged from 6 months

to 87 years with an average age of 26.48 ± 16.72 years. More than half of the victims (59.7%) were below 30 years. Table 1 summarizes the demographic and clinical profile of the snakebite victims.

About half of the snakebite victims were farmers or herdsmen who were bitten during their work (Table 1). The lower limb was the commonest site of bite (67.2%). More than half of bites (53.3%), with documented time of bite, occurred between the hours of 6 pm and 6 am. The median time elapsed from bite to hospital attendance was 8 hours, with a range of 20 minutes to 21 days.

Abnormal hemostasis (evidenced by abnormal bleeding or a deranged 20-minute whole blood clotting time) was present in 163 (84.9%) of the snakebite victims whilst 159 (82.8%) had local pain and swelling (table 1). Vipers were identified as the offending snake in 22 cases (about half of these were identified as the carpet viper *Echis ocellatus*) whilst a puff adder was implicated in one case.

Sixty-eight (35.4%) of the snakebite victims applied local medicine or herbs to the bite site (with or without scarification marks) prior to hospital attendance.

143

144 **Table 1: Demographic and clinical profile snakebite victims**

Variable		n (%)	Median (range)
Occupation	Farmer	89 (46.4%)	
	Herdsmen	5 (2.6%)	
	Student/pupil	56 (29.2%)	
	Housewife	10 (5.2%)	
	Unemployed	2 (1.0%)	
	Other	14 (7.3%)	
	Missing	16 (8.3%)	
Time of bite	6am-12 noon	17 (8.9%)	
	12noon-6pm	26 (13.5%)	
	6pm-12midnight	33 (17.2%)	
	12midnight-6am	16 (8.3%)	
	Missing	100 (52.1%)	
Place of bite	Farm/bush	93 (48.4%)	
	Outdoors (other)	41 (21.4%)	
	Indoors	31 (16.1%)	
	Missing	27 (14.1%)	
Site of bite	Upper limb	51 (26.6%)	
	Lower limb	129 (67.2%)	
	Trunk	1 (0.5%)	
	Missing	11 (5.7%)	
Gender	Male	131 (68.2%)	
	Female	61 (31.8%)	
Type of envenomation	Cytotoxic + Coagulopathy	139 (72.4%)	
	Cytotoxic only	20 (10.4%)	
	Coagulopathy only	24 (12.5%)	
	No Envenomation	9 (4.7%)	
First aid	Application of herbs	68 (35.4%)	
	Incision and suctioning	1 (0.5%)	
Age	<18 year	66 (34.4%)	
	≥18 years	125 (65.1%)	
	Missing	1 (0.5%)	
			23.0 (0.5-87.0)
Bite to hospital time (hours)			8.0 (0.3-504.0)
Duration of hospital stay (days)			4 (1-19)
Amount of antivenom administered (milliliters)			80 (0-380)

145 **Treatment**

146 No formal written protocol was followed in managing the snakebite cases. Treatment was mainly
147 based on the knowledge and experience of the attending doctor. Table 2 summarizes the
148 treatment received by the snakebite victims.

149 Anti-snake venom was administered in 94.8% of the snakebite cases with each patient receiving
150 on average 84.64 ± 59.35 milliliters (8 ± 6 vials). A lyophilized polyvalent antivenom supplied
151 by the Ministry of Health of Ghana was the main anti-snake venom used during the study period.
152 Twenty-six (13.5%) had documented reactions to the anti-snake venom administered. The
153 predominant route of administration was by intravenous infusion. A few patients who had
154 confirmed viper bites and were able to afford were given a monovalent *Echis Ocellatus*
155 antivenom with good results and minimal/no reactions.

156 Fresh frozen plasma (FFP) was used in addition to antivenin in patients with uncoagulable blood
157 or bleeding diathesis. About half (78) of those with clotting abnormalities received FFP; the
158 average number of units of FFP administered was 2.38 units. Thirty-eight patients (19.8%)
159 received whole blood transfusions.

160 Antibiotics were administered in almost all patients (99.5%). The commonest antibiotic was
161 flucloxacillin, which was used in 74% of snakebite victims, followed by amoxicillin/clavulanate
162 (used in 27.6%). More than half (51%) had at least two different antibiotics whilst 11.5% had at
163 least three different antibiotics.

164 Tetanus prophylaxis was given in about three-quarters of cases as tetanus toxoid (TT)
165 vaccination and anti-tetanus serum (ATS).

Analgesia was administered to 92.2% with more than half (55.7%) receiving paracetamol. Opioids were administered in about a quarter (25.5%) whilst 25 (13%) received a nonsteroidal anti-inflammatory agent (NSAID). Steroids were administered in 62%, mainly as intravenous hydrocortisone. Other medications given included vitamin K (28.6%), tranexamic acid (22.9%) and haematinic (15.6%).

Table 2: treatment administered

Treatment received	n (%)
Steroids	119 (62%)
Tetanus prophylaxis	TT 146 (76.0%)
	ATS 147 (76.6%)
Antibiotics	191 (99.5%)
Antifibrinolytics (tranexamic acid)	44 (22.9%)
Anti-snake venom	182 (94.8%)
Analgesia	177 (92.2%)
Vitamin K	55 (28.6%)
Haematinic	30 (15.6%)
Fresh Frozen plasma	80 (41.7%)
Whole blood	38 (19.8%)
Antihistamine	19 (9.9%)

184 Laboratory investigations

185 The 20-minute whole blood clotting time (20WBCT) was deranged in 155 (80.7%) of the
186 snakebite victims. Table 3 summarizes some laboratory indices of the snakebite cases.

Table 3: Summary of laboratory investigations

Laboratory test	N	Minimum	Maximum	Mean	Std. Deviation
Haemoglobin in g/dl	157	2.00	16.00	11.1796	3.14038
White cell count (x10 ⁹ /l)	157	1.95	554.00	13.8587	43.75062
Mean Cell Volume (fl)	150	57.00	107.00	81.2796	8.14234
Platelet count (x 10 ⁹ /l)	156	5	669	209.38	105.194
INR	6	.84	1.55	1.1450	.28773
AST in IU/L	35	9.00	73.00	32.0000	15.52940
ALT in IU/L	35	10.68	61.50	27.1340	12.79528
GGT in IU/L	33	7.90	86.90	31.6076	22.39791
ALP in IU/L	31	40.90	286.30	122.5419	66.88658
Protein in g/l	35	41.20	94.30	69.0331	12.66892
Albumin in g/l	35	27.10	61.00	39.6143	7.11370
Total Bilirubin in IU/L	35	4.79	90.05	17.2971	14.62767
Na in mmol/l	66	127.00	154.70	143.2152	4.94465
K in mmol/l	66	1.70	7.30	4.4336	.96810
Cl in mmol/l	65	90.00	124.90	104.1077	6.05370
S-Creatinine in umol/l	67	14.50	310.60	75.6904	39.85483
S-Urea in mmol/l	64	1.87	23.80	5.3155	3.26821

187 AST=serum aspartate aminotransferase; ALT=serum alanine aminotransferase; GGT=gamma glutamyl transferase; ALP=alkaline phosphatase;

188 INR=international normalized ratio; Na=sodium; K=potassium; Cl=chloride

189

Outcome and complications

The average length of hospital stay was 4.76 ± 2.965 days, with a range of 1 to 19 days (table 1). Three snakebite-related deaths were recorded during the study period giving a 1.6% mortality rate. Forty-nine (25.5%) patients were discharged with complications.

DISCUSSION

Snakebite is mostly a disease of rural farmers with the highest incidence recorded in Southeast Asia and Sub-Saharan Africa [1,21] and tends to afflict the economically active age group [22–25]. The nature of their occupation brings farmers, herdsmen and hunters [7,21] close to the natural habitat of these snakes. Most of the snakebites occur on the lower limb when the snake is accidentally trod upon by farmers without adequate protective footwear during farming activities [1,7]. We found that most of our snakebite victims were below 30 years of age and were bitten whilst engaged in farming activities. Late presentation to hospital characterizes snakebite cases in Africa [5,6]. Initial reliance on ineffective traditional remedies accounts partly for this late presentation. We found that at least a third of snakebite victims resorted to the use of traditional herbal remedies prior to presentation to hospital.

Identification of the snake species responsible for the bite allows likely course of the envenoming and potential complications to be anticipated and treated. This is usually difficult except when the dead snake is brought along to hospital. Envenomation by the carpet viper or saw-scaled viper (*Echis ocellatus*) results in a painful swelling of the bitten site which may result in tissue damage and necrosis [14]. The venom causes a consumptive coagulopathy as well as causing direct damage to the vascular endothelial basement membrane which may lead to a life-

212 threatening hemorrhage [14]. Almost all (95.3%) our snakebite victims presented with local
213 swelling and/or coagulopathy which is consistent with the envenomation pattern of the carpet
214 viper although a viper was identified in only 11.5% of the cases.

215 The World Health Organization's (WHO) guidelines on snakebite and its management in Africa
216 [1] are probably the most comprehensive guidelines available on the subject in this Region and
217 forms the basis for most local and institutional guidelines. Currently, a large number of
218 individual approaches are employed by doctors in the case management of snakebites in TTH
219 and other facilities in Ghana [19]. A study in India and Pakistan, two countries with high snake
220 bite mortalities, showed doctors were ill-prepared to handle snakebite cases [26]. Non-reliance
221 on local protocols results in a wide variation in the management principles employed in areas
222 such as the assessment of the severity of envenomation, dosage of antivenin used and the use of
223 ancillary medications. The implementation and adherence to a written protocol together with
224 staff training and patient sensitization have resulted in a significant reduction in snakebite
225 mortality in a rural hospital in Ghana [19]. These interventions resulted in improved health-
226 seeking behavior by shortening the average delay before presentation and ensuring an adequate
227 initial antivenom dose whilst limiting its excessive use [18,19]. Non-beneficial or potentially
228 harmful interventions are avoided by relying on evidenced-based guidelines whilst allowing a
229 more rational assessment of envenomation with clear endpoints to antivenom therapy.

230 The most important decision to be made concerning any patient presenting with a snakebite is
231 whether or not to give antivenom, the only specific antidote for snakebite [1]. Antivenoms may
232 be monovalent (against a single snake venom) or polyvalent (against venoms of several species
233 of snakes). The antivenom used during the study period is a polyvalent lyophilized equine
234 antivenom manufactured in India and supplied to the hospital courtesy the Ministry of Health of

235 Ghana. It is encouraging that antivenom was available to most of the patients who needed them.
236 The rate of use of antivenom and the number of vials administered in this study was higher than
237 that reported by another study in Ghana [27]. This disparity may be related to the relative
238 efficacy of the antivenoms administered or the fact that antivenom was freely available to
239 snakebite victims in this study.

240 The use of antivenoms is not without risks. Reactions ranging from mild to serious/life
241 threatening can result from their use and are particularly common with the polyvalent
242 preparations. Studies on premedication and adverse drug reactions have produced mixed results
243 [28,29]. Interventions that have shown some efficacy in reducing the frequency and severity of
244 anaphylactic reactions include premedication with intravenous hydrocortisone, antihistamines,
245 subcutaneous adrenaline and administration of a diluted antivenom by slow IV infusion over 60
246 minutes [28]. In the absence of compelling evidence of benefit, prophylaxis against allergic
247 reactions may only be considered in high risk individuals, that is, those with previous severe
248 reactions or have severe atopy [1,7]. Rigors and fever shortly after the infusion/injection was the
249 main adverse reaction to antivenom reported in this study. Almost two-thirds (62%) of patients
250 received steroids (mainly as intravenous hydrocortisone). It is not clear whether this was
251 administered as prophylaxis against allergic reactions to antivenom or as part of the treatment.
252 The widespread administration of steroids observed in this study is consistent with that found in
253 an earlier study in two district hospitals in Ghana [27]. Steroids per se are of no value in the
254 management of snakebites and may interfere with the venom- antivenom reaction [30].

255 Tranexamic acid was used in some of our patients (22.9%) to control coagulopathy. There is
256 little data on the use of antifibrinolytics in snakebite management. However, as in consumptive
257 coagulopathies due to other causes, the use of antifibrinolytics (without heparin) in envenomated

patients with coagulopathies may worsen outcome through their prothrombotic effects by causing microvascular thrombosis. Hence, the use of antifibrinolytics and heparin is generally discouraged in envenomated patients [1,7].

The use of prophylactic antibiotics in cases of snakebite is not appropriate [31–33] unless there are definite signs of infection or the wound has been grossly interfered with (such as incised with an unsterile instrument) or is necrotic. Most local effects of snakebite are attributable directly to cytolytic activities of the venom itself (rather than bacterial infection-mediated) so antibiotic treatment can be delayed in many cases. In one study, there was no difference in the length of hospitalization for patients with mild to moderate swelling (without necrosis or abscess) between those who were given antibiotics and those who were not [32]. All but one of the snakebite victims in this study (99.5%) received antibiotics. More than half of them (51%) received at least two different antibiotics whilst 11.5% received at least three different antibiotics. Studies in other parts of Africa have demonstrated a similarly high rate of routine prophylactic antibiotic usage [34].

A hospital-based study of snake bite always runs the risk of leaving out a significantly large group of patients who do not present to hospital for various reasons. A community-based approach would have helped overcome this limitation. Being a retrospective study, we were limited by the information documented in the patient folders, and this was compounded by the fact that no formal or written protocols were followed. For example, it was not clear on many occasions why steroids were administered, whether in anticipation of a drug reaction or as part of the management of the inflammation. A bigger study to explore the factors associated with adverse outcomes following snakebite in this environment may form the bases for an improved protocol for snakebite management in the country.

281 CONCLUSION

282 Snakebite is an occupational health hazard that affects mainly rural farmers. Healthcare
283 professionals still use non-guideline treatment approaches that may be harmful. Whilst
284 intensifying efforts at ensuring the continuous availability of effective antivenoms, there is the
285 need for the development and adherence to contextually relevant protocols that take into
286 consideration the prevailing local conditions. This will encourage the use of evidenced-based
287 approaches in snakebite management whilst avoiding the unwarranted use of non-beneficial
288 medications.

289

290 ACKNOWLEDGEMENT

291 We wish to thank Dr Sheila Owusu for her role in obtaining data from the Paediatrics
292 Department of TTH

293 FUNDING

294 No funding was received.

295 REFERENCES

- 296 1. World Health Organization. Guidelines for the Prevention and Clinical Management of
297 Snakebite in Africa. WHO Regional Office for Africa; 2010. 145 p.
- 298 2. WHO | Snakebite envenoming [Internet]. WHO. World Health Organization; 2017 [cited
299 2017 Dec 28]. Available from: <http://www.who.int/snakebites/en/>
- 300 3. Warrell DA. Snake bite. Lancet. 2010;375(9708):77–88.

- 301 4. Alirol E, Lechevalier P, Zamatto F, Chappuis F, Alcoba G, Potet J. Antivenoms for
302 Snakebite Envenoming: What Is in the Research Pipeline? de Silva HJ, editor. PLoS Negl
303 Trop Dis. 2015 Sep 10;9(9):e0003896.
- 304 5. Chippaux J-P. Estimate of the burden of snakebites in sub-Saharan Africa: A meta-
305 analytic approach. Toxicon. 2011;57(4):586–99.
- 306 6. Chippaux JP. Snake-bites: appraisal of the global situation. Bull World Health Organ.
307 1998;76(5):515–24.
- 308 7. World Health Organization. WHO/SEARO Guidelines for the clinical management of
309 snakebite in the Southeast Asian Region. Southeast Asian J Trop Med Public Health.
310 1999;30 Suppl 1:1–85.
- 311 8. Nasidi A. Snakebite as a serious Public Health problem for Nigeria and Africa. Presented
312 at WHO Consultative Meeting on Rabies and Envenomings: A Neglected Public Health
313 Issue, Geneva, Switzerland, 10 January 2007. 2007;
- 314 9. Molesworth AM, Harrison R, David R, Theakston G, Laloo DG, Reid A. Geographic
315 Information System mapping of snakebite incidence in northern Ghana and Nigeria using
316 environmental indicators: a preliminary study. Trans R Soc Trop Med Hyg. 2003;97:188–
317 92.
- 318 10. Warrell DA, Arnett C. The importance of bites by the saw-scaled or carpet viper (*Echis*
319 *carinatus*): epidemiological studies in Nigeria and a review of the world literature. Acta
320 Trop. 1976;33(4):307–41.
- 321 11. Pugh RN., Theakston RD. INCIDENCE AND MORTALITY OF SNAKE BITE IN

- 322 SAVANNA NIGERIA. Lancet. 1980 Nov;316(8205):1181–3.
- 323 12. Visser LE, Kyei-Faried S, Belcher DW, Geelhoed DW, van Leeuwen JS, van Roosmalen
324 J. Failure of a new antivenom to treat *Echis ocellatus* snake bite in rural Ghana: the
325 importance of quality surveillance. Trans R Soc Trop Med Hyg. 2008 May 1;102(5):445–
326 50.
- 327 13. Warrell DA. Unscrupulous marketing of snake bite antivenoms in Africa and Papua New
328 Guinea: choosing the right product—‘What’s in a name?’ Trans R Soc Trop Med Hyg.
329 2008 May 1;102(5):397–9.
- 330 14. Warrell DA, Davidson NMCD, Greenwood BM, Ormerod LD, Pope HM, Watkins BJ, et
331 al. Poisoning by bites of the saw-scaled or carpet viper (*Echis carinatus*) in Nigeria. Q J
332 Med. 1977 Jan;46(181):33–62.
- 333 15. Habib AG. Public health aspects of snakebite care in West Africa: perspectives from
334 Nigeria. J Venom Anim Toxins Incl Trop Dis. 2013 Oct 17;19(1):27.
- 335 16. Meyer WP, Habib AG, Onayade AA, Yakubu A, Smith DC, Nasidi A, et al. First clinical
336 experiences with a new ovine Fab *Echis ocellatus* snake bite antivenom in Nigeria:
337 randomized comparative trial with Institute Pasteur Serum (Ipser) Africa antivenom. Am J
338 Trop Med Hyg. 1997 Mar;56(3):291–300.
- 339 17. Warrell DA, Davidson NM, Ormerod LD, Pope HM, Watkins BJ, Greenwood BM, et al.
340 Bites by the saw-scaled or carpet viper (*Echis carinatus*): trial of two specific antivenoms.
341 Br Med J. 1974 Nov 23;4(5942):437–40.
- 342 18. Ghosh S, Maisnam I, Murmu BK, Mitra PK, Roy A, Simpson ID. A locally developed

- 343 snakebite management protocol significantly reduces overall anti snake venom utilization
344 in West Bengal, India. Wilderness Environ Med. 2008 Dec 1;19(4):267–74.
- 345 19. Visser L., Kyei-Faried S, Belcher D. Protocol and monitoring to improve snake bite
346 outcomes in rural Ghana. Trans R Soc Trop Med Hyg. 2004 May 1;98(5):278–83.
- 347 20. Ghana Statistical Service. 2010 Population and Housing Census: Regional Analytical
348 Report. 2013;9(8):3.
- 349 21. Harrison RA, Hargreaves A, Wagstaff SC, Faragher B, Lalloo DG. Snake Envenoming: A
350 Disease of Poverty. White J, editor. PLoS Negl Trop Dis. 2009 Dec 22;3(12):e569.
- 351 22. Raina S, Raina S, Kaul R, Chander V, Jaryal A. Snakebite profile from a medical college
352 in rural setting in the hills of Himachal Pradesh, India. Indian J Crit Care Med. 2014
353 Mar;18(3):134–8.
- 354 23. Rao CP, Shivappa P, Mothi VR. Fatal snake bites – sociodemography, latency pattern of
355 injuries. J Occup Med Toxicol. 2013 Mar 25;8(1):7.
- 356 24. Kshirsagar VY, Ahmed M, Colaco SM. Clinical profile of snake bite in children in rural
357 India. Iran J Pediatr. 2013 Dec;23(6):632–6.
- 358 25. Ghosh R, Mana K, Gantait K, Sarkhel S. A retrospective study of clinico-epidemiological
359 profile of snakebite related deaths at a Tertiary care hospital in Midnapore, West Bengal,
360 India. Toxicol Reports. 2018;5:1–5.
- 361 26. Simpson ID. A study of the current knowledge base in treating snake bite amongst doctors
362 in the high-risk countries of India and Pakistan: does snake bite treatment training reflect
363 local requirements? Trans R Soc Trop Med Hyg. 2008 Nov 1;102(11):1108–14.

- 364 27. Punguyire D, Baiden F, Nyuzaghl J, Hultgren A, Berko Y, Brenner S, et al. Presentation,
365 management, and outcome of snake-bite in two district hospitals in Ghana. *Pan Afr Med J*.
366 2014;19.
- 367 28. Caron EJ, Manock SR, Maudlin J, Koleski J, Theakston RDG, Warrell DA, et al.
368 Apparent marked reduction in early antivenom reactions compared to historical controls:
369 Was it prophylaxis or method of administration? *Toxicon*. 2009 Nov 1;54(6):779–83.
- 370 29. Williams DJ, Jensen SD, Nimorakiotakis B, Müller R, Winkel KD. Antivenom use,
371 premedication and early adverse reactions in the management of snake bites in rural Papua
372 New Guinea. *Toxicon*. 2007;49:780–92.
- 373 30. Blaylock RS. The identification and syndromic management of snakebite in South Africa.
374 *South African Fam Pract*. 2005;47(9):48–53.
- 375 31. Jorge M., Malaque C, Ribeiro L., Fan H., Cardoso JL., Nishioka S., et al. Failure of
376 chloramphenicol prophylaxis to reduce the frequency of abscess formation as a
377 complication of envenoming by Bothrops snakes in Brazil: a double-blind randomized
378 controlled trial. *Trans R Soc Trop Med Hyg*. 2004 Sep 1;98(9):529–34.
- 379 32. Blaylock RS. Antibiotic use and infection in snakebite victims. *South African Med J*.
380 1999;89(8):874–6.
- 381 33. Weed HG. Nonvenomous snakebite in Massachusetts: prophylactic antibiotics are
382 unnecessary. *Ann Emerg Med*. 1993 Feb;22(2):220–4.
- 383 34. Tagwireyi DD, Ball DE, Nhachi CF. Routine prophylactic antibiotic use in the
384 management of snakebite. *BMC Clin Pharmacol*. 2001 Dec 2;1(1):4.

385

386 **SUPPORTING INFORMATION LEGENDS**

387 S1 Dataset: Dataset supporting the findings of the study

388 S2 Checklist: STROBE checklist