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SURGERY IN LOW AND MIDDLE INCOME COUNTRIES

Surgical Considerations for Pediatric Snake Bites in Low- and Middle-Income Countries

Matthew C. Hernandez[1] · Michael Traynor[1] · John L. Bruce[2] · Wanda Bekker[2] · Grant L. Laing[2] · Johnathon M. Aho[1] · Victor Y. Kong[2] · Denise B. Klinkner[3] · Martin D. Zielinski[1] · Damian L. Clarke[2]

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Abstract

Background Snake envenomation is associated with major morbidity especially in low- and middle-income countries and may require fasciotomy. We determined patient factors associated with the need for fasciotomy after venomous snake bites in children located in KwaZulu-Natal, South Africa.

Methods Single institutional review of historical data (2012–2017) for children (<18 years) sustaining snake envenomation was performed. Clinical data, management, and outcomes were abstracted. Syndromes after snake bite were classified according to Blaylock nomenclature: progressive painful swelling (PPS), progressive weakness (PW), or bleeding (B), as it is difficult to reliably identify the species of snake after a bite. Comparative and multivariable analyses to determine factors associated with fasciotomy were performed.

Results There were 72 children; mean age was 7 (±3) years, 59% male. Feet were most commonly affected (n = 27, 38%) followed by legs (n = 18, 25%). Syndromes (according to Blaylock) included PPS (n = 63, 88%), PW (n = 5, 7%), and B (n = 4, 5%). Eighteen patients underwent fasciotomy, and one required above knee amputation. Nine patients received anti-venom. Few patients (15%) received prophylactic beta-lactam antibiotics. Hemoglobin < 11 mg/dL, leukocytosis, INR >1.2, and age-adjusted shock index were associated with fasciotomy. On regression, age-adjusted shock index and hemoglobin concentration < 11 mg/dL, presentation >24 h after snake bite, and INR >1.2 were independently associated with fasciotomy. Model sensitivity was 0.89 and demonstrated good fit.

Conclusions Patient factors were associated with the fasciotomy. These factors, coupled with clinical examination, may identify those who need early operative intervention. Improving time to treatment and the appropriate administration of anti-venom will minimize the need for surgery.

Level of evidence III

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✉ Matthew C. Hernandez
Hernandez.matthew@mayo.edu

Michael Traynor
traynor.michael@mayo.edu

John L. Bruce
johlbruce78@gmail.com

Wanda Bekker
drwiskeybravo@gmail.com

Grant L. Laing
grantlaing@me.com

Johnathon M. Aho
aho.johnathon@mayo.edu

Victor Y. Kong
victorywkong@yahoo.com

Denise B. Klinkner
klinkner.denise@mayo.edu

Introduction

According to the World Health Organization (WHO), nearly five million snake bites occur each year [1, 2]. Although less than half will result in envenomation, there are approximately 100,000 snake bite-related deaths annually [3, 4]. Additional sequelae include blindness or amputation [5–8]. Because of the extensive morbidity and mortality, the WHO deemed snake bites as a neglected tropical disease and a global health priority [9]. Current WHO-initiated protocols highlight optimal management [10], but fasciotomy is not routinely recommended because snake bite manifestations and severity can be clinically difficult to distinguish [11]. Subsequently, surgical decision making remains difficult after snake bite because of a lack of high-quality evidence that evaluates the need for interventions.

Sub-Saharan Africa is home to a number of venomous species of snake that humans may have contact with [12]. Poor infrastructure, long transfer times, and lack of access to appropriate anti-venom allow snake bites to remain an ongoing source of both morbidity and mortality in sub-Saharan Africa [13, 14]. In light of this, it is important to evaluate and optimize the surgical management of this injury [15]. This study evaluated snake bite injuries in children and adolescents in the western third of the KwaZulu-Natal province in South Africa with the purpose of identifying factors associated with the need for surgical intervention such as fasciotomy. We hypothesized that clinical and laboratory characteristics would be associated with the need for fasciotomy.

Methods

This is a single-institution review, and institutional review board approval was obtained prior to study. The ethics number is BCA 221/13. This study was performed at the Pietermaritzburg Metropolitan Trauma Service (PMTS), Pietermaritzburg, South Africa. The Hybrid Electronic Medical Registry (HEMR) was reviewed for the five-year period January 2012 to December 2017 [16, 17]. The PMTS provides definitive trauma care to the city of Pietermaritzburg, the capital of KwaZulu-Natal (KZN) province (Fig. 1). It is one of the largest academic trauma centers in KZN which also serves as the referral center for nineteen other rural hospitals within the province, with a total catchment population of over three millions [18].

All patients <18 years of age who were admitted to the PMTS service for the management of a snake bite were included in this study. Demographic data, admission physiology, and laboratory values were reviewed. Injury severity was measured using the Injury Severity Score (ISS) and age-adjusted admission shock index (heart rate/systolic blood pressure) [19]. Shock index cutoffs included >1.22 (age 0–6 years), >1.1 (age 7–12 years), and >0.9 (age 12–17 years). Details of the site of the snake bite, the type of syndrome, the clinical progression of the syndrome, the need for anti-venom, and need for operative management were recorded. The outcome of each operative intervention and all in-hospital morbidities were reviewed.

Management

The approach to managing snake bite is based on the syndromic approach which was popularized by Blaylock in 2005 [14, 20, 21]. This strategy recognizes that it is almost impossible to accurately identify the species snake which has bitten the patient and divides the management up into three recognizable clinical syndromes: progressive painful swelling (PPS), progressive weakness (PW), and bleeding (B). These correspond to the three venom types, namely cytotoxic, neurotoxic, and hemotoxic venom. According to Blaylock, the therapeutic triad includes: (1) elevation, (2) intravenous fluids, and (3) analgesia [22]. This combination is the mainstay of judicious conservative management for snake bites wherein the type of snake involved is unknown. Elevation of affected limb(s) provides analgesia and diminishes venous swelling, whereas intravenous fluids replace the intravascular fluid which extravasated into the tissues.

In addition to these basic supportive interventions, the selective use of anti-venom and operative interventions was considered. Anti-venom is needed for a subset of patients. In broad terms, the indications for anti-venom include complications of PPS, rapid respiratory deterioration following neurotoxic envenomation, or uncontrolled bleeding. Surgery is indicated mainly for the compartment syndrome of affected limbs, and debridement following tissue necrosis or secondary infection. This diagnosis of compartment syndrome is based on clinical findings: pain,

Martin D. Zielinski
zielinski.martin@mayo.edu

Damian L. Clarke
damianclar@gmail.com

1 Division of Trauma, Critical Care, and General Surgery, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

2 Department of Surgery, Pietermaritzburg Metropolitan Complex, University of KwaZulu-Natal, Pietermaritzburg, South Africa

3 Division of Pediatric Surgery, Mayo Clinic, Rochester, MN, USA

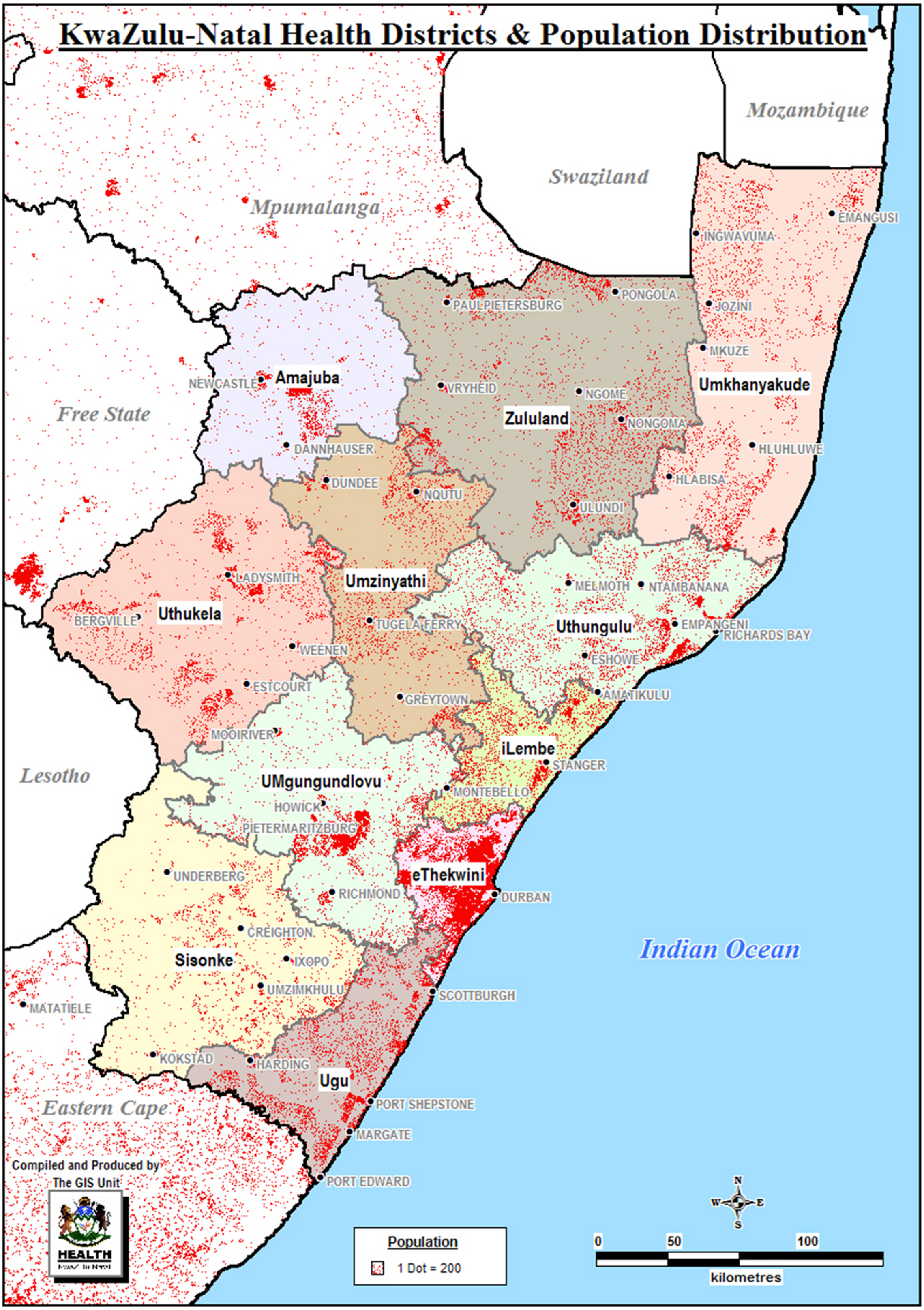

Fig. 1 Map of KwaZulu-Natal

paresthesia, paresis, pallor, pulselessness, and poikoilothermia [23]. Surgical interventions were performed after sequelae of hemorrhage or coagulopathy were corrected using blood product resuscitation.

Statistical analyses and outcomes

The primary outcome for this study was to determine patient factors associated with need for fasciotomy after a snake bite. Secondary outcomes included in-hospital complications, duration of stay, anti-venom utilization, and intensive care utilization.

Parametric data were described using mean with standard deviation (SD) and nonparametric data using median with interquartile ranges (IQR). Patients who underwent fasciotomy were compared to those who did not using Chi-square tests for categorical variables and independent *t* tests for continuous variables. Outcomes were stratified by Blaylock's snake bite syndromes. Two-tailed p values were considered significant ($\alpha < 0.05$). Multivariable logistic regression identified factors associated with fasciotomy. Covariates were selected based on clinical relevance and significance ($p < 0.05$) on univariate analyses. The multivariable analysis results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs) calculated using likelihood ratio tests. Model sensitivity and calibration were calculated. All data analyses were performed using JMP (SAS Institute Inc., Cary, NC).

Results

In this study, there were 72 children who sustained a snake bite. The mean (±SD) age was 7.7 (±3.6) years, the age range was 6 months to 15 years, and the majority were male ($n = 43$, 60%). The location of snake bites included: feet ($n = 27$, 38%), legs ($n = 18$, 25%), arms ($n = 15$, 21%), hands ($n = 9$, 12.5%), and head/neck ($n = 3$, 3.5%). The median (IQR) time from injury to admission to the hospital was 20 [11–31] hours, and the proportion of patients presenting to the hospital greater than 24 h after injury was 35%. Most patients had no comorbidity at the time of injury, one patient had a history of a prior snake bite (requiring hand debridement), and another was treated for tuberculosis. The clinical snake bite syndromes (according to Blaylock) included PPS ($n = 63$, 88%), PW ($n = 5$, 7%), and *B* ($n = 4$, 5%).

There were 35 patients (49%) that presented with an elevated age-adjusted shock index, and median volume of fluid administered at admission was 200 [50–500] cc of crystalloid. Two patients with head or neck bites required intubation at admission. Nine patients required anti-venom, and of these, two developed anaphylaxis requiring intensive care unit management. In total, ten patients (13.8%) were admitted to the intensive care unit. The median (IQR) duration of stay for the entire cohort was 5 [2–8] days. Twenty-five patients developed complications, and these are listed in Table 1. No patients expired.

Intravenous antibiotics were administered to 11 patients (15%), and these were derivatives of the beta-lactam family. Twenty-six patients (36%) were discharged with oral antibiotics. In Table 1, eight patients were readmitted with complications from infection (4 cellulitis, 3 abscesses, and a single case of sepsis). Patients were discharged frequently (93%) with medications for analgesia, and the agents most commonly prescribed were acetaminophen or ibuprofen. Follow-up was required in 22 (30.5%) of patients, and the remainder did not require formal follow-up.

Patient characteristics, management, anti-venom utilization, and outcome differences based on Blaylock's syndromes after snake bite are noted in Table 2. Between groups, there were no considerable differences with respect to injury severity or the presence of shock as measured by the age-adjusted shock index. There was a statistically significant, but clinically irrelevant difference in sex based on syndrome type. Physiologic and laboratory data were not substantially different between each syndrome type. A higher proportion of patients with PW and B demonstrated a hemoglobin concentration <11 mg/dL compared to patients with PPS. The administration of anti-venom was more frequent in patients with PW and B compared to PPS (Table 2). Further, there was a difference in the rates of fasciotomy; B patients were most likely ($n = 3$, 75%), followed by PW ($n = 2$, 40%), and PPS ($n = 13$, 20.6%). The duration of hospital stay was highest in the PW and *B* groups compared to the PPS.

A total of eighteen patients required fasciotomy. There were no considerable differences in patient age and sex between those who required fasciotomy and those who did not (Table 3). Patients who required fasciotomy demonstrated a higher median ISS compared to those that did not (9 [5–9] vs. 4 [4–4], $p = 0.008$). Additionally, fasciotomy patients were more likely to have tachycardia, elevated age-adjusted shock index, leukocytosis, hemoglobin <11 mg/dL, and INR >1.2. Patients with delayed presentation >24 h after snake bite more frequently required fasciotomy (83% vs. 27.7%, $p = 0.04$). The hospital resource utilization (duration of stay, anti-venom administration, and intensive care utilization) was higher in patients that required fasciotomy. Finally, the complication rates were higher in patients that required fasciotomy compared to those that did not (61% vs. 25.9%, $p = 0.01$).

There were no considerable differences between patients receiving anti-venom compared to those who did not based

Table 1 Complication types

Complication type	*N* (%)
None	47 (65)
Required skin graft	5 (7)
Cellulitis	4 (5.5)
Subsequent debridement	4 (5.5)
Abscess	3 (4.2)
Contracture	3 (4.2)
Anaphylaxis	2 (2.8)
Subsequent compartment syndrome	2 (2.8)
Pressure sore	1 (1.5)
Sepsis	1 (1.5)

on age, sex, injury severity, location of bite, or pulse; however, those that required anti-venom demonstrated lower admission systolic blood pressure (101 vs. 114, $p = 0.03$) and hemoglobin concentrations (9.9 vs. 12.4, $p = 0.01$). The median [IQR] duration of stay was prolonged in patients that required anti-venom (11 [6–18] vs. 4 [2–7], $p = 0.03$). The rates of complications were higher in patients that received anti-venom (66% vs. 30%, $p = 0.04$), and these patients also demonstrated a lower time from bite to admission (13 vs. 22 h, $p = 0.05$).

Results of the multivariable regression for patient factors that were independently predictive for fasciotomy are shown in Table 4. An elevated age-adjusted shock index, hemoglobin concentration < 11 mg/dL, delayed presentation >24 h after snake bite, and an INR >1.2 were independently predictive for fasciotomy. Age, injury severity, sex, and receipt of anti-venom were not associated with the need for fasciotomy. An elevated age-adjusted shock index was most predictive with the highest odds ratio. The model sensitivity was 0.89, and the Hosmer–Lemeshow test indicated good fit. The addition of anti-venom receipt into the model did not demonstrate a statistically significant reduction in the odds of fasciotomy.

Discussion

Snake bites and envenomation are a global health problem and a source of considerable morbidity for children [24]. Since management of snake bite is dependent on the type of envenomation and identification of the type of snake is seldom possible, the clinical management strategy is based on a syndromic approach [21]. Few data exist, however, to guide surgical management including fasciotomy [7, 11, 15, 25]. In this study, the majority of patients displayed a syndrome of PPS with few patients demonstrating PW or B syndromes. Differences in outcomes were noted based on the type of syndrome, with the worst outcomes in patients with PW or B syndromes. Patients with PW or B syndromes more frequently required anti-venom which suggests that severe syndromes were associated with higher hospital resource utilization and operative intervention.

Table 2 Overall patient characteristics stratified by syndrome

Characteristic	PPS *N* = 63	PW *N* = 5	*B* *N* = 4	*p*
Age (years)	6 [4–12]	7 [5–10]	9 [6–12]	.73
Male *n* (%)	41 (65)	1 (20)	1 (25)	.04
Injury Severity Score	4 [4–9]	9 [4–9]	7 [3–9]	.42
Elevated age-adjusted shock index *n* (%)	30 (48)	3 (60)	2 (50)	.86
>24 h after bite *n* (%)	21 (33)	1 (20)	3 (75)	.21
Heart rate (beats per minute)	112 [92–137]	134 [121–154]	119 [102–142]	.12
Systolic blood pressure (mmHg)	113 [101–121]	115 [95–117]	115 [93–127]	.94
Mean arterial pressure (mmHg)	82 [73–91]	85 [66–90]	78 [67–98]	.93
White blood cell count > 11 *n* (%)	33 (52.4)	3 (60)	3 (75)	.76
Hgb <11 *n* (%)	13 (20.6)	3 (60)	2 (50)	.05
INR >1.2 *n* (%)	27 (42.9)	2 (40)	3 (75)	.49
Duration of stay (days)	4 [2–7]	8 [6–11]	8 [2–21]	.04
Complications *n* (%)	21 (33)	3 (60)	1 (25)	.52
Need for intensive care *n* (%)	7 (11)	1 (20)	2 (50)	.06
Need for anti-venom *n* (%)	5 (7.9)	1 (20)	3 (75)	.003
Fasciotomy *n* (%)	13 (20.6)	2 (40)	3 (75)	.02

PPS progressive painful swelling, *PW* progressive weakness, *B* bleeding, *ISS* Injury Severity Score, *INR* international normalized ratio

Table 3 Overall patient characteristics in patients presenting after snake bite stratified by receipt of fasciotomy

Characteristic	Fasciotomy $N = 18$	No fasciotomy $N = 54$	*p*
Age (years)	6 [2–12]	8 [8–10]	.5
Male *n* (%)	66.6	57.4	.6
Injury Severity Score	9 [5–9]	4 [4–4]	.008
Elevated age-adjusted shock index *n* (%)	16 (89)	19 (35)	.0001
>24 h after bit *n* (%)	10 (55.5%)	15 (27.7)	.04
Heart rate (beats per minute)	141 [113–154]	104 [89–126]	.0003
Systolic blood pressure (mmHg)	117 [96–124]	113 [101–120]	.9
Mean arterial pressure (mmHg)	83 [72–92]	82 [73–89]	.64
White blood cell count >11 *n* (%)	16 (89)	23 (42)	.0006
Hgb <11 *n* (%)	10 (55.6)	8 (14.)8	.0005
INR >1.2 *n* (%)	12 (66)	20 (37)	.02
Duration of stay (days)	11 [5–16]	3 [2–6]	.003
Complications *n* (%)	11 (61)	14 (25.9)	.01
Need for intensive care *n* (%)	6 (33)	4 (7.4)	.001
Need for anti-venom *n* (%)	5 (27.8)	4 (7.4)	.003

These data highlight that considerable delay in treatment time and the presence of complicating envenomation factors like shock or bleeding were associated with an increased need for fasciotomy.

The syndromic approach to snake bite management was first employed by Blaylock [21]. The most common syndrome in our environment is PPS due to cytotoxic venom. The indications for anti-venom in patients with PPS include PPS which increases by more than 15 cm over an hour, PPS up to the elbow or knee 4 h after envenomation, PPS of the whole limb after 8 h, threatened airway, shortness of breath, associated clotting abnormalities, and a compartment syndrome [9, 10]. The administration of anti-venom is associated with a high rate of anaphylaxis [26, 27] as shown in the present study, and this may confound its usefulness when broadly applied to patients with snake bite and envenomation. Anti-venom must be administered in a high care setting under continuous monitoring and should be preceded by the administration of intramuscular adrenaline [5].

Table 4 Results of the multivariable regress for factors predictive of fasciotomy after snake bite

Characteristic	Odds ratio	95% confidence interval	*p* value
Elevated age-adjusted shock index	3.5	1.7–7.4	.001
Hemoglobin <11 mg/dL	2.5	2.3–2.7	.008
INR >1.2	1.7	1.1–4.8	.03
Presentation >24 h	3.1	1.2–7.8	.04

Sensitivity (area under the receiver operating curve): 0.89

Since patients with more severe disease states (PW and B) were associated with the need for anti-venom administration and fasciotomy, this suggests that clinical entities mandate vigilance during the initiation of supportive care [22, 28]. Need for fasciotomy is multifactorial; however, the results of the multivariable regression suggest that specific patient clinical and laboratory factors outside of a syndrome might be considered when estimating the need for operative intervention. The need for surgery is less well defined, and surgery is most commonly needed to manage a compartment syndrome (CS) of the limb [29]. CS remains a clinical diagnosis, and the clinical scenario in snake bite is clouded by the fact that the swelling may be confined to the subcutaneous fat and skin, not truly reflecting a compartment syndrome of the deep compartments [25]. Objective methods to diagnose a CS include direct measurement of the intra-compartment pressures and ultrasound [22, 25]. Measuring intra-compartment pressures is a painful, invasive, and cumbersome technique. The use of ultrasound to assess the state of the compartments has been described and is a painless and noninvasive technique, which requires further investigation.

In this series, the factors predictive of the need for fasciotomy included elevated age-adjusted shock index, hemoglobin (<11 mg/dL), delayed presentation >24 h, and elevated INR. Delays in transfer to a definitive center were also associated with increased likelihood of requiring a fasciotomy [30]. There is frequently a degree of crossover between cytotoxicity and hemotoxicity in these injuries.

This means that fasciotomy may result in catastrophic bleeding and should be preceded by the administration of anti-venom, especially in patients with low platelets or high INR [29]. Deranged clotting profiles or low platelets will be resistant to correction until anti-venom has been given. The most significant association with the need for fasciotomy is delay in transfer to a tertiary center [4, 31]. The issue around this is almost certainly one of delayed administration of anti-venom. Earlier referral and earlier administration of anti-venom may have averted the need for fasciotomy in a large proportion of these patients. This should be the focus of educational endeavors in the WHO's drive to reduce snake bite-related morbidity across the globe.

This study contains several limitations, foremost its retrospective nature. The sample size of this study limits the generalizability of the results, and application of the model to a larger cohort is warranted. The exact type of snake that bit each patient was unknown, limiting the ability to understand the type of venom. This was accounted for by describing patients snake bites in terms of clinical syndromes as elucidated by Blaylock. The timing of the administration of anti-venom was not recorded, and this limited the ability to discern this adjunct's impact on reducing the need for fasciotomy. In-patient fluid and blood product resuscitation volumes were not routinely recorded; therefore, it is difficult to ascertain whether conservative management using fluid resuscitation was effective. Despite these limitations, this study represents an accurate and current analysis of South African management and outcomes with pediatric snake bites and the results implicate the need for standardizing management using patient-specific clinical and laboratory parameters.

Conclusions

Snake bite is associated with significant morbidity in children including need for anti-venom administration and fasciotomy. Most patients in this series did not receive anti-venom, and this finding is likely unique to patients in low- and middle-income countries. Elevated age-adjusted shock index, hemoglobin <11 mg/dL, delayed presentation >24 h, and INR >1.2 may be useful in identifying patients who would benefit from early fasciotomy. Earlier referral may have averted the need for fasciotomy in a large proportion of these patients. Improving time to treatment or even access to anti-venom in rural settings might reduce the need for fasciotomy and complications of this procedure for patients with severe envenomation. These factors might be considered in surgical interventions after snake bite.

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Compliance with ethical standards

Conflict of interest The authors have no financial relationships or conflicts of interest relevant to this article to disclose.

Informed consent Informed consent was waived for participants within this study, and this was approved by the institutional review board.

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