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Chronic health effects and cost of snakebite

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ABSTRACT

The burden of disability among survivors and the socio-economic impact of snakebite have not been adequately researched. We reviewed original research articles, case reports and small case series relating to chronic physical, mental and psycho-social disability and economic burden of snakebite. Both physical and psychological health problems seem common in snakebite survivors and can lead to disability and loss of productivity. Chronic physical health effects, musculoskeletal disability being the commonest, can be largely attributed to limited and delayed access to optimal treatment of acute envenoming. The economic burden is considerable, and includes health system costs, out-of-pocket expenditure and opportunity costs, with regional variations. Health systems should be more responsive to needs and circumstances of bite victims, and a more holistic approach should be developed in the treatment of snakebite which incorporates the management of chronic health effects.

1. Introduction

Snakebite envenoming causes significant morbidity and mortality in tropical and subtropical countries in Africa, Asia, Oceania and Latin America (Kasturiratne et al., 2008). Most of the morbidity and mortality occurs in young adults living and working in farming and other labour intensive occupations in impoverished rural areas. The combination of poor access to often sub-optimal health services, scarcity of effective and safe antivenom, and the burden placed on families and communities due to snakebite victims with disability, many of whom are young and economically productive, is very likely to result in a considerable medical, social and economic toll (Hansdak et al., 1998). Despite their importance, neither the burden of disability among survivors nor the socio-economic impact of snakebite have been adequately researched.

Most snakebite-related research is focussed on the epidemiology and clinical aspects of acute envenoming and mortality, which understandably take priority in countries struggling with inadequate resources to manage and save the lives of snakebite victims. Although recommendations have been made that assessments of snakebite burden should include chronic disability and related socio-economic costs, obtaining reliable data on these aspects is challenging. There are several reasons for this. Snakebite envenoming mainly occurs in the poorest regions of the world (Harrison et al., 2009) and the available data are usually based on incomplete hospital returns or central databases (Kasturiratne et al., 2008). Snakebites are often underreported because many victims may seek traditional treatments, either due to preference or inadequate or absent allopathic treatment facilities (Pugh et al., 1980; Snow et al., 1994; Rahman et al., 2010; Ediriweera et al., 2017). Furthermore, there is rarely, if ever, routine follow-up of snakebite victims who are discharged from hospital after the acute complications of envenoming have resolved and, with loss of further contact, the allopathic system fails to detect possible longer-term disabilities and their consequences.

In Asian, African and Latin American countries, there are many studies which report that health workers lack sufficient knowledge and confidence in snakebite management (Fung et al., 2009; Sapkota et al., 2020; Inthanomchanh et al., 2017; Gajbhive et al., 2019). The problem stems from deficiencies in the training of these professionals in their medical or nursing courses (Inthanomchanh et al., 2017; Kharusha et al., 2020). Chronic disability following snakebite is more likely to occur, both, where there is poor access to healthcare and in situations where management of the bite is inadequate. In such settings follow-up of victims is extremely unlikely to occur.

While improved medical management has the potential to reduce chronic physical disability, for example, reduce the rate of limb amputations or severe disfigurement, psychological disability following a snakebite may yet occur (Williams et al., 2011). Adverse physical effects of envenoming are related to the necrotoxic, neurotoxic and hematotoxic damage caused by venom components, but the mechanisms by which snake envenoming causes psychological disability has not been explored.

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Although the allopathic system, in general, loses contact with snakebite victims after their discharge from hospital, some survivors can, and do, continue to seek help from traditional healers who are easy to access and offer them social and psychological support which takes into account the religious and cultural beliefs of local communities. Research on chronic disability following snakebite may, therefore, benefit from the inclusion of traditional healers (Stienstra et al., 2021).

In this paper we review the available published literature on chronic physical, mental and psycho-social disability and economic burden of snakebite.

2. Methods

2.1. The search strategy

This review was conducted according to the PRISMA 2020 statement for reporting systematic reviews (Page et al., 2021). To identify original research papers published on chronic health effects of snakebite, we searched PubMed, Scopus and EBSCOhost databases using the terms "snake bite" OR "snakebite" AND "health effects" OR "morbidity" OR "disability" OR "sequelae" OR "consequences" AND "long term" OR "chronic" OR "delayed". This search resulted in 1247 research papers. 829 remained after duplicates were merged. Of these, 229 were book or book sections. Remaining 600 journal articles and thesis were screened using the abstract and 41 and 75 were excluded due to being animal studies and reviews, respectively. The remaining 484 publications were screened for relevance and content. PubMed, EBSCOhost and Scopus databases and the specific journals websites were used to retrieve the full papers. 472 full papers and 12 abstracts were retrieved and reviewed. 59 papers contained data on chronic health effects of snakebite (Fig. 1). Health outcomes prevalent at the time of discharge from the hospital and reported as persistent at least 4 weeks after discharge and outcomes attributed to the index snakebite that occur after discharge from the hospital and persist for a minimum of 4 weeks from discharge were considered.

We conducted a separate search in PubMed, EBSCOhost and Scopus (limited to subject areas: Medicine and Economics, Econometrics and Finance) databases using the terms "snake bite" OR "snakebite" AND "economic" OR "cost" OR "expenditure" OR "burden". This search resulted in 1855 scientific publications. 1523 remained after duplicates were merged. 96 book chapters and book sections were excluded. Remaining 1427 papers were evaluated for relevance through screening the abstract. This resulted in identifying 325 potentially relevant publications. 318 full papers and 7 abstracts were reviewed to identify 15 papers describing the out-of-pocket expenditure or the cost of snakebite for the health system at hospital, country or regional level (Fig. 2).

3. Results

We reviewed 59 original research papers to identify information on chronic health effects of snakebite and 15 papers that dealt with its cost.

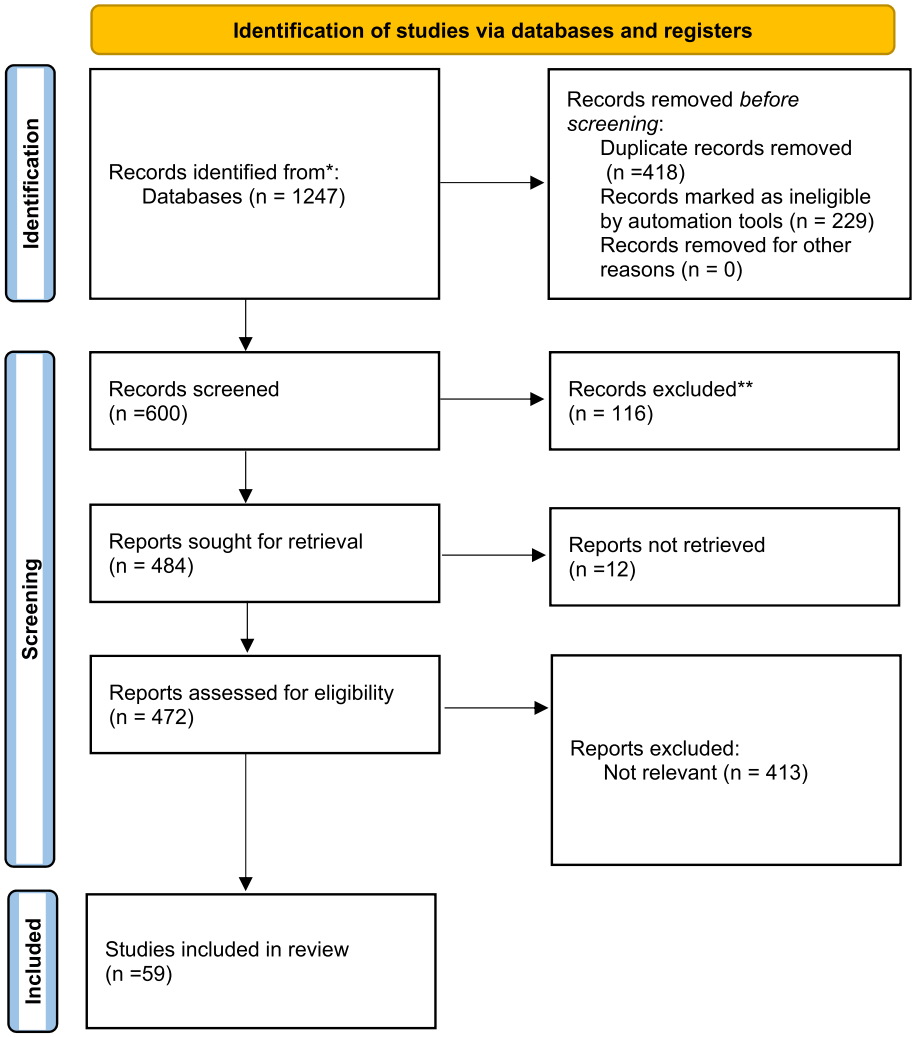

Fig. 1. PRISMA 2020 flow diagram for reviewing the chronic health effects of snakebite.

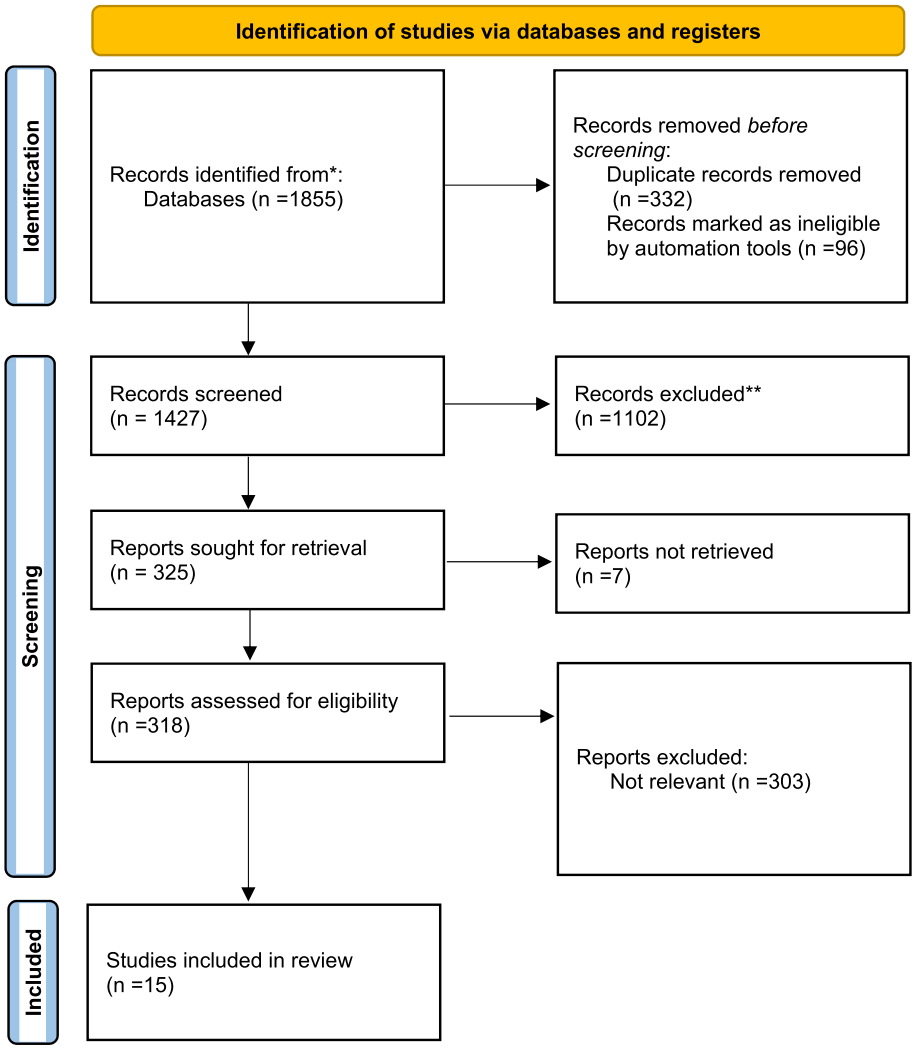

Fig. 2. PRISMA 2020 flow diagram for reviewing the cost of snakebite.

3.1. Chronic health effects of snakebite

Chronic or long-term health effects of snakebite has many definitions in the available literature. They include, any condition related to snakebite that required follow-up after discharge from hospital, conditions that last or appear more than six weeks following envenoming, or health problems that had occurred immediately or within 4 weeks of the bite and had persisted for more than 3 months (Williams et al., 2011; Jayawardana et al., 2018; Waiddyanatha et al., 2019; Brenes-Chacon et al., 2020).

Chronic physical health effects of snakebite can be broadly classified into dermatological, musculoskeletal, neurological, renal and endocrine conditions. Chronic psychological health effects include a broad group of mental health problems. These are summarized in (Table 1).

3.2. Chronic physical health effects

Skin blistering after snakebite envenoming often results in the development of necrotic lesions which are difficult to treat, especially in the context of poorly resourced health care facilities in areas where snakebite is common, where surgical expertise and antibiotics are in short supply and hospital conditions favour secondary infection. Chronic non-healing ulcers and persistent or recurrent blisters at the bite site, though rare, are the most commonly reported dermatological conditions (Jayawardana et al., 2016; Jayawardana et al., 2018). Hypertrophic scars, which may cause contractures leading to disfigurement and functional limitations even requiring reconstructive surgery, and hyper-pigmentation and discolouration of skin in the affected part of the body, have also been commonly reported. Excessive hair loss has also been reported rarely. Musculo-skeletal disabilities are the commonest chronic condition associated with snakebite. Weakness, functional limitation and deformities of the affected limbs due to muscle dystrophy are commonly reported (Caiaffa et al., 1994; Jayawardana et al., 2016; Rodríguez and Gutiérrez, 2019). Tissue necrosis leading to amputation of parts of the affected limb is the most severe and debilitating chronic condition associated with snakebite globally [Kidmas et al., 2004; Tsai et al., 2017]. There does not seem to be consistency in the use of surgical techniques emphasizing the need for standardization (Sachett et al., 2020b).

A migraine-like syndrome characterized by headache, blurred vision, nausea and dizziness has been described (Jayawardana et al., 2018). Other neurological conditions with long-lasting impact such as visual and hearing impairment, paresthesia at the bite site, and persistence of hemiparesis or hemiplegia due to cerebrovascular events at the time of acute envenoming have also been reported (Spano et al., 2014; Jayawardana et al., 2018). Chronic renal failure requiring haemodialysis has been reported in some victims of snakebite who had developed acute kidney injury following the bite (Naqvi, 2016; Pucca et al., 2020). Establishing causality is challenging as most of these reports provide no information regarding the victims' renal function prior to envenoming,

Table 1
Chronic health effects of snake bites.

No	Authors	Location	Long term health effects	
			Physical	Psychological
1	Caiaffa et al. (1994)	Southeast Brazil	• Muscle contractures • Amputations • Chronic renal failure	Not reported
2	Sharma et al. (2004)	South Eastern Nepal	• Scar with deformity • Chronic wound	Not reported
3	Kidmas et al., 2004	Jos, Nigeria	• Gangrene • Amputation	Not reported
4	Bell et al. (2010)	Teaching Hospital, Kurunegala, Sri Lanka	• Abnormal nerve conduction	Not reported
5	Williams et al. (2011)	North Central Province, Sri Lanka	• Blindness • Tooth decay • Body aches • Headaches • Tiredness • Weakness.	• Depressive disorder • Post-traumatic stress disorder
6	Khosrojerdi and Amini (2013)	Imam Reza Hospital, Iran	Not reported	• Post-traumatic stress disorder
7	Spano et al. (2014)	UCSF-Fresno Medical Education Program Medical Centre, Fresno Central California	• Localised pain at bite site • Numbness/paraesthesiae • Abnormal skin peeling and discolouration • Persistent weakness of the bitten extremity	Not reported
8	Wijesinghe et al. (2015)	District General Hospital, Polonnaruwa, Sri Lanka	Not reported	• Depression • Anxiety
9	Habib et al. (2015)	Northeastern Nigeria	Not reported	• Post-traumatic stress disorder • Impaired family/school functioning • Psychological morbidity
10	Jayawardana et al. (2016)	Ampara, Sri Lanka	• Local pain in affected limb • Swelling of affected limb • Muscle wasting • Chronic non-healing ulcer • Chronic lump • Reduced muscle power • Reduced range of motion • Balance impairment • Abnormal gait • Fixed deformities • Amputation	Not reported
11	Naqvi (2016)	Sindh Institute of Urology and Transplantation, Karachi, Pakistan	• Chronic kidney disease	Not reported
12	Tsai et al., 2017	Chia-Yi Chang Gung Memorial Hospital in Taiwan	• Necrotizing fasciitis	Not reported
13	Islam et al., 2017	Rangamati Sadar Hospital, Rangamati, Bangladesh	• Numbness • Severe asthenia • Tingling • Generalized pain •Localised pain	• Depression • Post-traumatic stress disorder • Anxiety
14	Naik et al. (2018)	Chandigarh, India	• Chronic pituitary failure	Not reported
15	Yerawar et al. (2020)	Nanded, India	• Hypopitiutarism	Not reported
16	Proby et al. (1990)	London, UK	• Anterior Pituitary Faliure	Not reported
17	Jayawardana et al. (2018)	Ampara, Sri Lanka	• Migraine-like syndrome • Musculoskeletal disorders • Visual impairment • Chronic renal failure • Skin blisters at the bite site • Hemiplegia • Facial palsy • Local paresthesia • General shivering • Chronic non healing ulcer • Hearing loss • Excessive hair loss • Lassitude with body aches • Abdominal colic • Chest tightness • Wheezing • Receding gums	• Psychological distress
18	Arias-Rodríguez and Gutiérrez (2020)	South-eastern (Brunca region) Costa Rica	• Functional limitation of affected limb • Amputation	• Anxiety • Depression • Post-traumatic stress disorder
19	Brenes-Chacon et al. (2020)	National Children's Hospital in Costa Rica	• Hypertrophic scars needing skin graft • Functional limitation of affected limb • Deformity	Not reported

(*continued on next page*)

Table 1 (*continued*)

No	Authors	Location	Long term health effects	
			Physical	Psychological
			• Amputation	
20	Sachett et al. (2020a)	Brazil	• Disability in mobility	• Poor cognition • Disability in self-care, getting along, impact in life activities, participating in society
21	Pucca et al. (2020)	Las Claritas Bolívar, Venezuela	• Chronic Kidney Disease	Not reported
22	Pulimaddi et al. (2017)	India	• Chronic Kidney Disease	Not reported
23	Priyamvada et al. (2019)	Puducherry, India	• Chronic Kidney Disease	Not reported
24	Alcoba et al. (2020)	Akonolinga health district, Centre Region, Cameroon	• Amputation of distal phalanges • Ankylosis of phalanges • Tingling • Chronic recurrent pain	• Subjective psychological trauma
25	Kumar et al. (2018)	Malabar, North Kerala, India	• Hypopituitarism • gangrene and amputation • Osteomyelitis • Intracranial hemorrhage and cerebrovascular accidents	Not reported
26	Brenes et al. (2018)	National Children's Hospital, Costa Rica	• Chronic lymphedema, • Functional impairment	Not reported
27	Pérez-Gómez et al. (2019)	Western Brazilian Amazon	• Haemorrhagic stroke	Not reported
28	Sachett et al. (2020a)	Guajará (Amazonas state), Western Brazilian Amazon	• Haemorragic stroke	Not reported
29	Kim et al. (2021a)	Chungnam National University Hospital, Daejeon, Korea	• Skin necrosis • Rhabdomyolysis	Not reported
30	van Oirschot et al. (2021)	Kajiado and Kilifi counties. Kenya	• Pain and numbness • Weakness or paralysis of the bitten area • Scarring • Amputation or permanent disability • Recurrent swelling • Recurrent wounds • Dizziness • Sleeping and breathing problems • Functional disability	Not reported
31	Kularatne (2002)	Anuradhapura, Sri Lanka	• Nerve conduction defects • Sensory loss at the site of bite • Bilateral ulnar nerve palsy with wasting of small muscles of the hands • Sensory motor neuropathy • Cerebella ataxia	
32	Corneille et al. (2006)	Texas, USA	• Amputation	Not reported
33	Yates et al. (2010)	Meserani, Tanzania	• Amputation	Not reported
34	Herath et al. (2012)	Kandy, Sri Lanka	• Chronic Kidney Faliure	Not reported
35	Namal Rathnayaka et al., 2020	Sri Lanka	• Chronic Kidney disease	Not reported
36	Seneviratne and Dissanayake (2002)	Ratnapura and Polonnaruwa, Sri Lanka	• Peripheral sensory loss	Not reported
37	Elbey et al. (2017)	Diyarbakır, Turkey	• Amputation	Not reported
38	Weinstein et al. (2018)	Australia	• Amputation	Not reported
39	Zeng et al. (2019)	Chongqing, P.R. China	• Skin necrosis • Rhabdomyolysis	Not reported
40	Halilu et al. (2019)	Sub-Saharan Africa	• PTSD • Amputations	Not reported
41	Gerardo et al. (2019)	Southeastern United States	• Functional disability	Not reported
42	Banerjee et al. (2019)	India	• Cerebella ataxia	Not reported
43	Lizarazo et al. (2020)	Catatumbo, Colombia	• Cerebral hemorrhage	Not reported
44	Srirangan et al. (2020)	Kalubowila, Sri Lanka	• Gangreen leading to amputation • CRF	Not reported
45	Habib et al. (2021)	North-eastern Nigeria	Not reported	• Posttraumatic stress disorder • Poor QoL in psychological and social domains • Impaired family/school functioning • Psychological morbidity
46	Kazemi et al. (2021)	Iran	• Fasciotomy related long term morbidity	Not reported
47	Jelinek et al. (1998)	Nedlands, Western Australia	• Renal insufficiency	Not reported
48	Chroni et al. (2005)	Rion-Patras, Greece	• Neuropathy	Not reported
49	Sinha et al. (2009)	Kolkata, India	• Chronic Kidney Disease	Not reported
50	Golay et al. (2014)	West Bengal, India	• Chronic Kidney Disease • Hypopituitarism	Not reported
51	Mahmood et al. (2018)	Mandalay Division, Myanmar	• Chronic renal failure • Chronically infected bite site wound • Hypopituitarism • Loss of a limb from amputation	Not reported
52	Lee and Yao (2010)	Arizona, USA	• Stenosing flexor tenosynovitis	Not reported
53	Bonasso et al. (2015)	West Virginia, USA	• Osteonecrosis at bite site	Not reported
54	Gelman et al. (2021)	Texas, USA	• Septic arthritis at bite site	Not reported

(*continued on next page*)

Table 1 (*continued*)

No	Authors	Location	Long term health effects	
			Physical	Psychological
55	Dhabhar et al. (2021)	India	• B/L axonopathic Optic neuritis	Not reported
56	Pérez-Gómez et al. (2019)	Western Brazilian Amazon	• Haemorrhagic stroke • Temporal hemianopsia • Headache • Tissue necrosis • Retinal haemorrhages • Skin ulcers • Visual defects • Hemipareisis	Not reported
57	Abraham et al. (2020)	Kerala, India	• Muscle and joint weakness	Not reported
58	KIm et al. (2021b)"	Republic of Korea	• Local tisssue necrosis • Scarring	Not reported
59	Gupta et al. (2021)	Delhi, India	• Neuromuscular weakness	Not reported

and therefore the problem is neglected. Hypopituitarism and resulting disturbances in related hormones has been reported in snakebite victims lasting for many years after the bite (Naik et al., 2018).

3.3. Delayed psychological effects

Delayed psychological effects following snakebite have been poorly investigated. Depressive symptoms and post-traumatic stress disorder are the most common psychological conditions reported following snakebite (Khosrojerdi and Amini, 2013; Williams et al., 2011). Non-specific somatic manifestations of psychological problems resulting from the experience of snakebite, which may be related to socio-cultural beliefs that promote a sick role are also described in the literature (Rodríguez and Gutiérrez, 2019; Alcoba et al., 2020).

3.4. Cost of snakebite

The estimations of the cost of snakebite in the literature are summarized in Table 2.

The available estimates cover health system costs and out-of-pocket expenditure of snakebite (Hasan et al., 2012), and the burden of snakebite (Habib et al., 2015). The cost per death averted has been estimated for 16 countries in West Africa (Hamza et al., 2016). Using data on mortality and amputations, the total burden of snakebite in West Africa has been estimated at 320,000 DALYs (95% CI: 248,000–403,000 DALYs) per year with Nigeria accounting for 43% of the burden (Habib et al., 2015).

In Cameroon, the relatively expensive prices of AVS ranging from US $20–75 are unaffordable for households of the most vulnerable communities (Tochie, 2017). Clinical protocols developed for standardization of antivenom use has been effective for reducing the cost of care, by reducing the number of vials used and the length of hospital stay, with no significant difference in complication rates (Ghosh et al., 2008; Weant et al., 2012). However, in many regions in Africa, including Cameroon, the antivenoms have not been tested for effectiveness, and the efficacy of the antivenoms used is questionable. This issue needs to be addressed as a priority (Potet et al., 2019).

Regional variations in the cost of care and the disease burden have been described within the most affected countries and across regions over the last 20 years (Kasturiratne et al., 2005; Habib et al., 2015; Curran-Sills and Kroeker, 2018).

4. Discussion

Snakebite is a debilitating condition both from a health and economic perspective (Habib and Brown, 2018). As the condition is most prevalent in the most vulnerable populations living in low-income countries and, in addition to development of adverse chronic health effects, the extra cost incurred by a snakebite may have a devastating economic impact on the victims and their families (Harrison et al., 2009). In this paper, we reviewed the available literature on the chronic health effects and costs of snakebite envenoming.

Chronic health effects of snakebite, though likely to be commoner than reports indicate, have received limited attention in the snakebite literature. The wide variation in the definition of "chronic health effects" in relation to their point of appearance and duration, indicates the lack of a systematic approach to defining and describing this very important aspect of snakebite (Williams et al., 2011; Jayawardana et al., 2018; Waiddyanatha et al., 2019; Brenes-Chacon et al., 2020). Screening and detection of chronic disability related to snakebite would require at least one out-patient follow-up visit after victims are discharged from hospital. The development of a set of patient-centred outcomes, based on the available evidence and expert consensus, would make the assessment for chronic disability and its management more systematic and meaningful.

The reported chronic physical health effects of snakebite can be largely attributed to delayed or lack of access to appropriate treatment, and inappropriate or sub-optimal treatment within health facilities due to limited resources or poor quality of care. Although "400,000 disabilities caused by snakebites each year worldwide" is often cited in the recent literature, how this number was arrived at or details regarding the severity, offending species and which regions are worst affected are sparse.

The most commonly reported is musculoskeletal disability. Persistent limb swelling, probably the result of lymphatic or vascular injury, has been reported, especially after viper bites; 8/800 snakebites in Sri Lanka (Jayawardana et al., 2016), 19% after Malayan pit viper bites in Thailand (Wongtongkam et al., 2005). While most dermatological and musculo-skeletal damage, especially those related to venom related tissue necrosis, may lead to disfigurement, surgical interventions such as fasciotomy and amputations to treat compartment syndrome and subsequent tissue necrosis have life-long consequences with severe disability and loss of productivity (Habib et al., 2015). Doppler Ultrasound is a useful tool to evaluate swelling and exclude compartment syndrome (Ho et al., 2021) and where available, may be a promising approach to avoid unnecessary fasciotomy. Another relatively simple intervention maybe physiotherapy, which is rarely done after snakebite, but will probably significantly improve the outcome and reduce the number and severity of chronic musculoskeletal disorders. At present there does not seem to be consistency in the use of surgical techniques, and standard protocols are urgently needed.

Psychological problems may occur even after "successful" treatment of snake envenoming with AVS, and although difficult to detect without adequate follow-up, together with associated non-specific somatic manifestations, can have considerable negative social and economic impacts, for example, from loss of employment (Williams et al., 2011). A small randomized trial of a brief psychological intervention, that can be provided by non-specialist doctors, appeared to reduce psychiatric

Table 2
Cost of snakebite reported in global literature.

Health system cost of snakebite			
No	Author	Location	Cost
	Lopoo et al. (1998)	USA	• US$2450 per child treated
	Hasan et al. (2012)	Bangladesh	• Total expenditure of snakebite: US$4- US$2294 (Mean = US$124). • Mean income loss: US$93. • Expenditure for venomous snakebite: US$231 • Expenditure non-venomous snakebite: US $34
	Saz-Parkinson et al. (2012)	Spain	• Mean: Euro2000 per case
	Narra et al. (2014)	33 children's Hospitals in Pediatric Health Information System, USA	• Patients receiving anti-venom under observation status: US$17665 • In-patients receiving anti-venom: US$20503
	Kasturiratne et al. (2017)	Sri Lanka	• Annual estimated health system cost: US $10,260,651.53 • Cost of anti-venom: US $6.3 million • Cost of hospital care: US $3.9 million
	Tochie (2017)	Cameroon	• Cost of an AVS vial: US $67–75 or US$20–23
	Okumu et al., 2019	JOOTRH, Kisumu County, Western Kenya	• The median cost of treating snakebite: 2652 KES (US$26).
	Magalhães et al. (2020)	Brazilian Amazon	• Health system cost: US $3.115.861,28. • The total cost: US$8 million in 2015
	Benabdellah et al. (2020)	Children's University Hospital of Rabat, Morocco	• The average direct medical costs: US$127/child • The average direct non-medical costs: US$30/child
	Khan et al. (2020)	Saudi Arabia	Direct healthcare cost per snakebite patient by severity category • Mild: SAR 15,005 (Mean = SAR 3750) • Moderate: SAR 87,707 (Mean = SAR 29,444) • Severe: SAR 92,286 (Mean = SAR 46,143) • Death: SAR 43,142 (Mean = SAR 43,142) • Total: SAR 238,140 (Mean = SAR 26,460)
Household cost of snakebite			
No	Author	Location	Cost
	Sharma et al. (2004)	South eastern Nepal	• Household cost: US$69 (SD = 100)
	Vaiyapuri et al. (2013)	Tamil Nadu, India	• The direct cost (transport and medical expenses): Rs.0–350,000 (£4858).
	Kasturiratne et al. (2017)	Sri Lanka	• National direct out-of-pocket expenditure for snakebite: US$1,981,699
	Magalhães et al. (2020)	Brazilian Amazon	• Cost from the patient's perspective: US$268 914.18.
Burden of snakebite			
No	Author	Location	Cost
	Habib et al. (2015)	Nigeria	• The cost/death averted: $2330.16 • The cost/DALY averted: $99.61 (discounted) and $56.88 (undiscounted)
	Hamza et al. (2016)	West Africa	The cost/death averted for Guinea Bissau: US$1997 The cost/death averted for Liberia and Sierra Leone: US $6205 The cost/DALY averted for Benin Republic: US$$83 (95% Confidence Interval: US$36-$240) The cost/DALY averted for Sierra-Leone: US$281 ($159–457).
	Kasturiratne et al. (2017)	Sri Lanka	• Total number of DALYs for envenoming and death: 11, 101–15,076 per year • For males 5624–7927 DALYs • For females 5477–7150 DALYs • The total DALYs (snakebites without envenoming) - 20–500 per year • Total annual economic burden of snakebite: US $14,097,789
	Quintana-Castillo et al. (2020)		• Cost-effectiveness ratio (CER) of treatment with AV for each death avoided: US$1253 • Cost-effectiveness ratio (CER) of treatment with AV per DALY avoided US $51
	Magalhães et al. (2020)	Brazilian Amazon	• The estimated cost due to premature death: US $3031 300.38. • The cost attributed to the loss of productivity: US $1539 518.62.

symptoms and disability related to family and social life after snakebite envenoming, but not depression or post-traumatic stress disorder (Wijesinghe et al., 2015). More research is required to develop culturally-appropriate interventions for those affected, especially focusing on post-traumatic stress disorder and depression following snakebite.

There has been an increase in the number of studies reporting economic burden of snakebite over the last ten years (after 2010). Out of pocket expenditure and opportunity costs incurred by victims and their families have been reported in several studies (Vaiyapuri et al., 2013; Kasturiratne et al., 2017; Magalhães et al., 2020). Hospital based studies commonly report the cost of care for a single episode of snakebite. Although there are wide variations in the cost across the regions of the world, developing treatment protocols may help to reduce the cost of care as well as the rates of complications that may lead to chronic disability (Ghosh et al., 2008; Weant et al., 2012). National level studies on the economic burden of snakebite and studies on the cost-effectiveness of anti-venom treatment have highlighted the problem of limited availability of AVS and the financial burden placed on poorer economies where snakebite is common, due to the cost of AVS.

In conclusion, poor healthcare and limited access to anti-venom are the leading causes of morbidity and chronic disability due to snakebite envenoming. These can adversely impact the economy of poor communities. Health systems need to be more responsive to the needs and circumstances of the victims of snakebite, developing a more holistic approach that incorporates the management of the acute manifestations of envenoming, preventing mortality, together with management of

chronic health effects, both physical and psychological. Chronic health effects of snakebite and the economic cost of snakebite are inter-related and are a part of a vicious poverty cycle that deserves the highest attention of snakebite researchers, administrators and policy makers.

Author contributions

AK: conceptualization, literature survey, writing the first draft, revision of the manuscript. DGL: conceptualization, revision of the manuscript. HJdeS: conceptualization, writing the first draft, revision of the manuscript. All three authors approved the final version of the manuscript.

Ethical Statement

"Chronic health effects and cost of snakebite":

1) This material is the authors' own original work, which has not been previously published elsewhere.
2) The paper is not currently being considered for publication elsewhere.
3) The paper reflects the authors' own research and analysis in a truthful and complete manner.
4) The paper properly credits the meaningful contributions of co-authors and co-researchers.
5) The results are appropriately placed in the context of prior and existing research.
6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.
7) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

The violation of the Ethical Statement rules may result in severe consequences.

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I agree with the above statements and declare that this submission follows the policies of Toxicon as outlined in the Guide for Authors and in the Ethical Statement.

Declaration of competing interest

All three authors have no conflict of interests to declare.

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