FACTORS THAT INFLUENCE CLINICAL OUTCOMES OF SNAKE BITES WITH SPECIAL REFERENCE TO SUPPLY OF ANTI-SNAKE VENOM AND RELATED DRUGS AT KILIFI COUNTY REFERAL HOSPITAL IN COASTAL KENYA

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A thesis submitted in partial fulfillment of the requirements for the award of the Degree of Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance ,

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DEDICATION

I dedicate this work to my wife for the support she has given me throughout the study period.

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LIST OF ABBREVIATIONS

ASV	Antisnake venom
CHMT	County Health Management Team
CIDP	County Integrated Development Plan
DRSABCDE	Danger,Response, Send for help, Airway, Breathing, Cardiopulmonary resuscitation, Disability of nervous system and Environment
FGD	Focus Group Discussion
KCH	Kilifi County Hospital
KEMSA	Kenya Medical Supplies Authority
NTD	Neglected tropical diseases
WHO	World Health Organization

ABSTRACT

Background: Envenomation with snake venom is one of the life threatening hazards affecting people residing in the tropics. World Health Organization (WHO) recognized snake envenomation as one of the important Neglected Tropical Disease (NTD) conditions in the year 2017.

Objective: The main objective of the study was to determine the distribution, types, seasonality and management of snake bites at Kilifi County Referral Hospital in coastal Kenya.

Methods: This retrospective study was conducted at the Hospital pharmacy and the health records office of Kilifi County Hospital by extracting data from patient files and pharmacy records. The demographic and clinical data was obtained from the files using a standardized data collection tool. Descriptive statistics were used to determine prevalence, frequencies, means and standard deviation. Multivariate logistic regression was conducted to assess the relationship between the ASV use and selected predictor variables.

Results: The study established that snake bites are more prevalent in June and December of every year. Out of a total of 255 cases of snake bite cases identified, there was no mortality despite the fact that only 19% had been treated with anti-snake venom (ASV), no victim received adrenaline as part of treatment while 67% received hydrocortisone injection. Only one patient was scheduled for amputation of which he declined to give consent. The average admission period was 2 days. The only available anti-snake venom was the polyvalent type. Non-steroidal anti-inflammatory drugs were widely used to treat pain related with snake bites (63.1%), despite the risk of hemorrhage. There was no stock out of ASV, hydrocortisone and adrenaline injections in the pharmacy.

Conclusion: The prevalence of snake bites was varying throughout the study period, with the peak being around June and December of each year. All the required drugs and anti-snake venom were available in the pharmacy. There was no snake-bite related mortality during the study period. More concerted public health effort should be put in place to prevent, identify and manage snake bites during the peak period of June to December every year.

CHAPTER ONE: INTRODUCTION

Background

Snake envenomation is one of the reasons for admission and hospitalization as an in-patient or outpatient at Kilifi county referral hospital(1). With a doctor: population ratio of 1 to 42,625, snake envenomation puts the population of Kilifi county at high risk of mortality or dilapidating outcomes (1).

The problem of snake bites affects many countries all over the world with South East Asia and Africa having the greatest burden of snake bites (2). This is due to the fact that apart from findings snakes in their natural habitat, human beings are increasingly keeping snakes as pets in their homes in the western world and also in zoos as part of their collection (2). WHO also states that Snake bites mostly affect people residing in the tropics and Asia (3). In the tropics, where snakes are generally found in their natural habitat, snake envenomation mainly happens when humans interact with these reptiles during their daily chores or when the reptiles stray into their homes in search of food and shelter (4). Outcomes from snake envenomation range from mortality, physical disabilities, prolonged hospitalization which leads to high medical costs to the victim, and untold psychological suffering (5). In some instances, snake bites are associated with witchcraft and bad luck and can lead to serious conflicts within the community(6). In Africa, there are more than 315,000 snake bites envenoming annually with 7,000 amputations, and 32,000 deaths (6).

The supply of anti-snake venom and related drugs in management of snake bites is highly critical in determining clinical outcomes especially in circumstances where envenomation is evident(7). With onset of devolution in the 2010 Constitution of Kenya, every citizen has the right to the highest attainable standards of health (8).To attain this standard, supply of pharmaceuticals plays a vital role(9).

The supply chain for pharmaceuticals and other consumables in health is one of the Seven Pillars in the public health system that is vital to provision of services as stipulated in the WHO health systems strengthening (10). However, as much as there has been a lot of interest in quantifying and documenting the general pharmaceutical supplies in public healthcare, there is scarcity of information regarding supply of medicines and medical supplies targeting management of snake bites(11).

In Kenya, there is scanty information on dynamics and patterns in service delivery surrounding management of snake bite cases with little information on supply of anti-snake venom and related drugs - hydrocortisone, adrenaline, blood products and other medicines for pain management and prophylaxis against infections in cases of snake bites(4).

Statement of the Problem

Inhabitants of Kilifi County are at risk of snake bites given that the vast territory of this county is mostly rural with subsistence farming and animal rearing being main economic activity (12). The warm climatic condition of the coastal strip also makes it a suitable snake habitat. More than 800,000 residents of Kilifi County residing in rural areas are at risk of suffering snake bites (13). Snake envenomation is a big public health problem in Kilifi County due to vast impact on socio-economic structure of the population occasioned by loss of life, finances lost to medical bills and permanent disability that occur in some cases of snake envenomation (6). Families lose income through death of breadwinners, payment of medical bills, disability and loss of man-hours during hospitalization (14). Mortality from snakebites is also not well documented due to limited data and little research in this important area of public health(14). Despite WHO designating snake bites as one of the neglected tropical disease conditions in June 2017, Kilifi county hospital has had challenges in management of snake bites coupled with scanty data on snake bite cases(15). The situation isn't made better by the fact that majority of victims still seek alternative modes of treatment such as application of the black stone, traditional herbal medicine, laceration and sucking of the wound, and prayers as identified in other places within the country (16).

Research Questions

a) What is the proportion and distribution pattern of snake bites at Kilifi County Hospital (KCH) during the study period?

b) What was the monthly/seasonal variation in the number of snake bite cases?

c) From WHOs syndromic classification, what were the common types of snakes that cause envenomation in patients with snake bite at Kilifi County hospital?

Main Objective

The main objective of this study was to determine the distribution, types, seasonality and management of snake bites at Kilifi County Referral Hospital in coastal Kenya.

Specific Objectives

Specifically, the study sought to:

a) To determine distribution in person and place and proportionate morbidity and mortality of snake bites at Kilifi County Referral Hospital in coastal Kenya from 2013 to 2017

b) To determine monthly/seasonal variation in the number of snake bite cases within the study period.

c) To classify snakebite cases at the hospital using WHO system-according to syndromic manifestation of the victims

Study Justification

Envenomation with snake venom in set-ups without adequate supply of ASV and skills in management of snake bites can lead to various undesirable outcomes for the victim(15). Kilifi County reported the third highest prevalence of snake bites in Kenya Health Information System (KHIS) – formally District Health Information system (DHIS2)- in the year 2016(17). However, there is no documented records that shows at what time of the year inhabitants of this county are most at risk of getting bitten by snakes(18). There was also no documented data showing the pattern and distribution of snakebites within the county. Therefore this information was highly critical for planning purposes.

Significance of the Study

The study was a first step in establishing the magnitude of the problem and the supply of medication used in management of snake bites. This study was to inform health initiatives towards management of snake bites in the county and also be critical in development of guidelines and strategies to reduce snake bites. The study also provided invaluable information for stakeholders involved in control of snakebites, which is one of the neglected tropical diseases. The study sought to inform stakeholders interested in supply of commodities aimed at combating snake bites on the time of the year when the commodities were most needed. This information is crucial in helping avoid wastage of the vital but expensive ASVs through expiries. The information is also critical in avoiding overstocking of this medicine, thereby reducing misuse of financial resources.

The findings from the study are highly informative during planning, control and management of snakebites since they lead to establishment of prevalence of the problem and the shortage of medication that are essential in management of the same. They also inform the health facility managers on which type of anti-venom to stock, the need for hydrocortisone, adrenaline and other related medicines.

It was also imperative to note that general information on snake bites is overally un-available or scanty due to lack of tools from the Ministry of Health to collect data in this area. Therefore, findings from this study was to stir the Ministry of Health into generating reporting tools to capture information on outcome of snake bites in victims who were hospitalized. With scarcity of information on dynamics surrounding management of snake bite cases, this study attempted to bridge that gap in order to provide information on supply

of anti-snake venom and snake envenomation. Therefore, it is highly important to establish the magnitude of the problem and supply situation of anti-snake venom and other drugs used in management of snake envenomation. The findings are also a great step towards raising awareness on this neglected tropical disease. The awareness will eventually lead to development solutions to challenges facing proper management of the same(1)

These findings are also helpful for the national program that was in charge of combating snake bites, the Neglected Tropical Disease Program (NTD), to develop timely strategies and interventions in combating the menace within the Coastal region, especially Kilifi County(15). The Ministry of Health can also use these findings to improve on the public health training packages for health workers, community health volunteers and community sensitization to manage or reduce exposure to snake bites per year.

The study was also helpful in filling the information gaps regarding outcome of snake bite cases at this hospital, supply of ASV and related drugs, monthly incidences and other challenges as part of information required by the County Government, the Ministry of Health and other stakeholders involved in NTD control. The gaps addressed included lack of information on annual seasonal variability in snake bites, clinical outcomes, use of ASV, the improper management of snake bites and residential areas within the county with highest number of snake bites which ought to be given priority in public health initiative to reduce incidences of snake bites. Therefore, the information obtained is crucial in policy and development of guidelines geared towards reducing in incidences and management of snakebites

CHAPTER TWO: LITERATURE REVIEW

Introduction to Snake Bites

Snakes are carnivorous reptiles that are elongate and legless and belong to the sub-order Serpentes, which are cold-blooded animals that inhabit almost all regions in the world except Antarctica and some islands that include: Iceland, Greenland, and Hawaiian Archipelago (20). When a snake bites another animal or human being, it inflicts an injury called a Snakebite that may or may not develop into a wound(21). There are between 1.5 to 5.5 million snake bites cases reported in the world every year(22). There are 421,000 to 2.5 million cases that result into envenomations which lead to 20,000 to 125,000 deaths annually (3). Snake bites are a global phenomenon with South-Eastern Asia and Sub-Saharan Africa being two regions that report high incidence rates(23). India reports the highest number of cases per year, due to the favorable climatic conditions which promote snake reproduction and proliferation (22). Most of the snake bite cases are due to occupational hazard e.g. in snake handlers, some due to keeping snakes as pets or working within habitats of snakes (23). In Kenya there are 127 identified snake species, but just 18 are known to be venomous and 6 are capable of causing death in humans((16), (24)). Snakes inhabit land as well as water bodies where there are Sea Snakes (25). They are ectotherm amniote vertebrates covered with overlapping scales, and they evolved from lizards more than 140 million years ago (26). Their skulls are made up of several mobile joints that allow them to swallow pray several times bigger than their heads(27). They do not have external ears and their internal organs are arranged one after another instead of side by side along the elongated body and move by using specialized scales laterally, rectilinearly, concertinally and by sidewinding (28). They also have only one functional lung and another one which is a vestigial lung(26). There are 20 identified families of snakes with 520 genera and 3600 species in total(29). A majority of snakes are not venomous (30). The venom is purely used to subdue prey and self-defense in cases where the snake is threatened (31). Snake venom is modified saliva that consists of complex proteins substances like enzymes, peptides, and amino acids and it is stored in a gland in the head of the snake (19). The venom is ejected via the ducts into hollow fangs (teeth) into the prey or victim upon a bite (32). The components of snake venoms consist of hyaluronidase enzyme which aids its spread and numerous toxins: neurotoxins (attack nervous system) and hemotoxins (destroy red blood cells) (33). Also contain bungarotoxins, cytotoxins and many other toxins that are toxic to the nerve tissue (34).

There are only three taxonomic families of snakes that have been documented to be venomous. These families have been identified to be: Viperidae consisting of vipers,rattlesnake, etc; Elapidae like green mamba, cobras, etc and Hydrophidae which are sea snakes(35). However, not all sea snakes are poisonous (2)..

For medical purposes, WHO has classified envenoming snakes that are found in Africa into five categories as shown below (2):

Category 1: Bite frequently with dilapidating outcomes/ serious/life-threatening envenoming eg sow scaled or carpet viper, Somali puff adder (*Bitis arietans somalica*), Egyptian Carpet Viper (*Bitis Leakayi*, around Lake Baringo), Spitting or cytotoxic cobras of genus *Naja*, Neurotoxic cobras of the same genus, green Mamba (genus *Dendroaspis*), Black mamba (*D. polylepis*) (2)

Category 2: These are Snakes which bite frequently but do rarely cause any serious or any life-threatening envenoming: African burrowing asps (Genus *Atractaspis.*), African Night adder(Genus *Causus*): snouted night adder (*C. Defilippi*), Litchenstein's Adder/ olive green night adder (*C. litchensteini*), western Rhombic night adder (*C. maculatus*), Eastern rhombic night adder (*C. rhombeatus*), one found in North Africa called the Sand Viper or also the desert horned adder (a member of the Genus *Cerastes*): the Saharan Horned viper (*C. cerastes*), the sand viper of Sahara also called the Saharan sand viper (*C. vipera*) (2).

Category 3: These are Snakes which bite rarely but can cause life-threatening or serious envenoming: they include the Boomslang (genus *Dyspholidus)*, tree snake (*Thelotornis spp*), South-Eastern Savanna vine snake(*T. capensis*), twig snake (*T. kirtlandii*), Montipellier snake (*Malpolon monspessulanus*) (2).

Category 4: Theseare Snakes that are known to bite rarely and are not known to cause any serious envenoming: other neurotoxic cobras: *N. anchietae*, *N. melanoleuca* (this include the forest black and white-lipped cobra), Rinkhals (*Haemachatus haemachatus*), desert black snake or cobras or the Walter Innes's snake (scientifically known as *Walterinnesia aegyptia*), the Yellow-bellied snake found in the sea (sea snake) (*Pelanis platurus*), also the Bush snake (tree viper) (of the Genera *Atheris Proatheris, montatheris, and Adenorhinos* –which include the Mt Kenya bush viper *A. desaixi*), Gaboon adder (*B. rhinoceros, B. gabonica*), Lowland/ swamp or flood viper (*Poatheris superciliaris*), dwarf adders (genus Bitis), Side winding adder(B. peringuey), Coral or shield-nosed snake(Genus *Aspidelaps – A. lubricus lubricus, A. scutatus*…), Moorish viper (*Macrovipera mauritanica*)(2)(18).

Category 5 snakes are the other potentially venomous ones that have not caused any known or documented bites (2).

Mechanism of Toxicity

More than 90% of snake venom is proteins, comprising of enzymes, polypeptides and some non-harmful proteins like nerve growth factor(43). Enzymes make up 90% of venom content in Viperid and 25-75% in Elapids ((23), (44)). The toxic digestive enzymes include hyaluronidase, hydrolases and activating factors like the L-amino acid oxidase enzyme, phosphomonodiesterase enzymes, 5- nucleotidase enzyme, DNAase enzyme, NAD-Nucleosidase enzyme, Phospholipase A2 enzyme and the peptidase enzymes (2).

Hyaluronidase promotes the spread of the venom by breaking down tissue structure(45)

The Zinc metalloproteinase haemorhagin enzymes act by breaking down vascular endothelium leading to profuse bleeding (34).

Pro-coagulant enzymes extracted mostly from Viperids, some Elapids and Collubrids contain Serine protease which activates factor X, prothrombin and other clotting factors that induce the formation of fibrin in the bloodstreams(34). However, the resultant clots are then broken down by fibrin within the body and this leads to depletion of clotting factors within thirty minutes which eventually lead to profuse bleading. Some viperids like Russell's viper contain toxins which activate factor V, IX, X and XIII leading to fibrinolysis, platelet aggregation, anticoagulation, and hemorrhage (46).

Phospholipase A2 (lecithinase) toxin causes damage to the mitochondria, the red blood cells, leucocytes, nerve endings in the peripheral body system, skeletal muscle cells, vascular endothelium, and platelets (34). This toxin also produces sedative effects that mimic opiates effects, also induces massive release of histamine and anticoagulation of blood (34).

Proteolytic enzymes (that are mainly Metalloproteinases or hydrolases) and the released cardiotoxins increase permeability of vascular walls causing edema, bruising and blistering (2).

The polypeptide in the venom has neurotoxins that act at the postsynaptic junction such as -bungarotoxin, and α-cobrotoxin which do bind onto the acetylcholine receptors resulting into a blockage(46). Other toxins like β-bungarotoxin, taipoxin, and crotoxin are large peptides 120 – 140 amino acids with Phospholipase A ending which damages the presynaptic junction (46).

How severe the envenoming episode will present depends on the content of the venom, volume of venom injected into the victim and site of the bite (46). Therefore smaller or younger snakes may cause severe damage than bigger or older snakes due to a higher concentration of particular toxin(s) (47).

Signs and Symptoms of Snake Envenoming

Only 20% to 50% of bites by known venomous snakes result into envenomation (48). Toxicity of snake venom can be broadly classified into four according to clinical effects recorded upon envenomation of a victim: cytotoxic e.g. puff adders, neurotoxic e.g. black mambas, mixed cytotoxic and neurotoxic e.g. rhinkals and haemotoxic e.g. boomslang (4).

WHO has summarized signs and syndromes of snake bite envenoming as shown below (2):

Syndrome 1 presents as localized envenoming with bleeding/clotting disturbance. This is common in all Viperidaes (11).

Syndrome 2 includes local envenoming that result into bleeding, followed by shock, and acute renal damage. This occurs commonly in bites by Russell's Viper (which is also known as the hump-nosed viper) that is found in Sri Lanka and South-Western India (46).

Another symptom is occurrence of conjunctival edema sometimes accompanied by acute pituitary insufficiency. This is typical in envenoming by Russell's viper found mostly in Myanmar (46).

In some envenomation ptosis, external ophthalmoplegia, and also facial paralysis with dark-brown urine can occur (46). Such cases have been reported in Sri Lanka and SW India

Syndrome 3 commonly present as swelling accompanied by paralysis. This is common in cobra and mamba envenoming ((11), (14)).

Syndrome 4 includes paralysis with minimal local swelling. If the victim was bitten on land the snake might be a krait bite, but if the occurred in the Ocean, estuary or water body, it is most likely due to sea snake envenoming (46).

Syndrome 5 occur as paralysis with an acute renal injury characterized by dark brown urine common with Rusell's viper, krait or sea snake envenomation (46)

Effects of Snake Envenomation:

Acute

Effects of snake bite can be due to local envenoming, affecting the site of the bite, Systemic envenoming affecting body organs – these two scenarios can lead to permanent disability and anxiety ((34), (49)). Sometimes the effects of the envenoming are amplified by the anxiety of the victim. This anxiety can lead to an increase in respiratory rate, palpitations, elevated blood pressure, tetany of limbs, dizziness, profuse sweating and apprehension (50). Most of the incidences, the snake may not be venomous (51).

Most of the time traditional first aid such as tourniquet application, lacerating snakebite site, sucking, application of heat at the bite site and amputation can result in more damage than good ((50), (52)).

However, acute sign of snake envenoming is instant pain that may be throbbing, bursting or burning due to the bite followed by swelling of the site (soft pitting edema), bullae and subsequent tenderness and inflammation of lymph nodes proximal to the site of the bite (if the bite is on the lower limb femoral or inguinal lymph nodes will be inflamed, on the elbow-epitrochlear lymph nodes, upper limb-axilla lymph nodes) (39). Bite by Cobra, sea snake or krait may be painless with negligible local swelling (4).

Local signs at the bite site include visible fang marks, localized pain, bleeding at the site of the bite, bruising, inflammation, lympharyngitis with subsequent lymph node enlargement, necrosis, putrefaction/rotting and abscess formation that may require debridement (2).

Generalized systemic symptoms include nausea, vomiting, malaise, weakness, abdominal pain, and prostration (2).

The cardiovascular symptoms that are common with viperid envenoming include visual disturbance, faintness, collapse, shock hypotension, pulmonary edema and conjunctival edema (chemosis) (34).

A bleeding disorder which present as spontaneous and systemic in nature present as hemoptysis, conjunctivitis, intracranial hemorrhage and cerebral thrombosis that can easily lead to coma and stroke respectively (46). Also rectal bleeding or melaena, hematuria, per-vaginal bleeding, antepartum hemorrhage in pregnancy, and skin, mucosal and retinal bleeding (2). Seen mostly in Viperidae

Neurological disorders include drowsiness, ptosis, and altered taste of smell, external opthalmoplegia, facial muscles paralysis and also numbness of other muscles(53). Regurgitation through the nose, opthalmoplegia, aphonia, and difficulty in swallowing secretions may arise coupled with generalized flaccid paralysis leading to accumulation of saliva, drooling and impaired swallowing mostly seen in Elapidae bite victims(2).

Skeletal muscle breakdown is characterized by excruciating pain, trismus, myoglobinuria, and hyperkalemia which can culminate into acute renal failure and cardiac arrest(46). These symptoms are common in sea snake envenoming(46).

Renal symptoms are characterized by lower back pain, hemoglobinuria, anuria, myoglobinuria, and uremia whose symptoms include acidotic breathing, some hiccups, nauseating feeling, and sometimes accompanied with pleuritic chest pain (54).

Endocrinological symptoms include acute pituitary/adrenal insufficiency due to anterior pituitary infarction(54). The acute phase of endocrinal insufficiency may lead to shock and hypoglycemia

Chronic signs

Tissue loss due to debridement leading to scarring, amputation or chronic ulceration, infection, contractures, arthrodesis or chronic arthritis leading to physical deformity and disability(11). Malignant transformations have also been seen in some cases (34, 5).

Cobra spit can lead to permanent blindness due to corneal scarring, laceration, and secondary endophthalmitis (34).

There are reported cases of renal failure after bilateral cortical necrosis (viper), chronic panhypopituitarism, and diabetes insipidus (46).

Chronic hyponatremia due to increased permeability of capillaries has been recorded in krait poisoning (46).

Snake envenoming has been recorded to eventually lead to amputation of limbs due to severe gangrene and necrosis and muscle strictures leading to physical disability (2).

The most surprising sequellae from snake envenomation is hypo-pituitary that lead to loss of secondary sexual hairs, that culminated into hypogonadism, loss of sexual libido, with amenorrhea in females, testicular atrophy in males, and hypothyroidism that has been recorded in some Asian countries (46).

Treatment and Management

Some of the documented traditional treatment of snake bites in Kenya include the application of the black stone (snake stone) at the site that was bitten, bloodletting or cuts, herbal concoctions including ashes made from snakeheads, cow dung and herbs, witchcraft and others (53), (39). Some of these treatments can cause more harm than good, therefore they should not be a reason to delay taking the victim to a hospital (41).

First aid:

Recommended first aid to a victim of snake bite should be done following the DRSABCDE protocol. The acronym D stands for danger, R for response, S for send for help, A for secure the airway, B for breathing, C for Cardio-pulmonary resuscitation, D for Disability of the nervous system- continue assessing level of consciousness, and E for protection from environmental factors like strong sunshine, rain-water and cold (51).

The limb that has been bitten should always be elevated above the level of the heart (41). The victim should then be reassured to keep calm and laid down as you call for help, then the

aider should apply pressure bandage above the bite site as soon as possible, if it is available, noting the time of the bite (55). The crepe bandage should be applied as tightly as possible starting from the fingers/toes and to cover the entire beaten limb (90% of snake bites occur on the limbs). A piece of cloth or any other bandage can be used if crepe bandage is unavailable. The limb should be immobilized by applying a sling or splint and the patient should be kept still during transportation to the hospital. If using a motorbike to transport a patient to a hospital, a pillion passenger should be available to support him or her (46). The aim of first aid is to reduce further spread of the venom, control distressing signs of envenoming and preserve life. Application of the pressure pad should be avoided in cases where the bite is from an elapid snake, like the black mamba as this can lead to permanent paralysis. Application of very tight tourniquets, incision at the site of the bite, suction of blood and application of ice packs are all discouraged (56). Tourniquets applied for long periods, for more than 40 minutes, can lead to ischemia (46). Apply ABCDE protocol of first aid at all times.

There should be no attempt to kill the snake due to the risk of getting bitten, but if the snake is dead, it should be taken to the hospital in a sealed container for identification and eventual administration of specific ASV for the victim (53). Touching dead snakes should be avoided, since even a severed head can bite (57).

Venom spit should not be washed from the clothes or unbroken skin since it can be used as a sample to identify the snake where such services are available (57).

One can administer paracetamol to reduce pain, but the time of dosing should be noted (51). Use of NSAIDS in snake bite victims should be avoided due to the risk of hemorrhage (58).

Medical intervention

Whether one requires medical intervention depends on how severe the outcome of the envenomation is(11). Cases of severe tissue necrosis may lead to amputation of the limb(s), fasciotomy and skin/tissue grafting (39). Administration of antibiotics for prophylaxis, steroids and tetanus toxoid are also advocated (59). However, administering the anti-snake venom (ASV) in cases of snake envenomation where it is available is the most definitive treatment (35).

Anti-snake venom (ASV) comprises immunoglobulin G (in most cases it is the pepsin refined Fab-2 fragment of the whole IgG) obtained from the plasma of horses, mules or donkeys (equine) and sheep (ovine) (47). The antivenom can be monovalent or polyvalent(53). It should only be used where benefit outweighs the risk, and in cases of severe and systemic envenomation due to risk of anaphylaxis (60). Skin or conjunctival hyper-sensitivity test can

be conducted before administration but however, this test shouldn't be used to delay treatment since it doesn't predict the early or late reaction to the ASV(54). The route of choice for the administration of antivenom is the slow intravenous route (53). There must be a drawn vial of adrenaline/ epinephrine in anticipation of an anaphylactic reaction (31).

In cases of neurotoxic envenoming with bulbar and respiratory paralysis, artificial ventilation to avoid death by asphyxiation should be availed (53).

Fasciotomy and debridement should be avoided in cases with bleeding or hemostatic abnormalities until this is rectified and high intracompartmental pressure or syndrome is established by direct measurement (46). The simplest test to assess for clotting is the 20-minute test(34). It involves getting a sample of whole blood to assess for blood coagulability. It helps guide medical personnel on the viability of surgical interventions (2).

Other medication that should be at hand when administering ASV is Adrenaline to mitigate against possible anaphylaxis, pain should be managed by paracetamol or an opioid analgesic and blood or blood products should be used as a treatment in cases of envenomation with haemotoxic venom (39, 45).

The main limitations in locally available anti-snake venoms is that they are all imported and that they are developed based on venom from non-local snakes (46). They are therefore not specific for local envenomation and therefore some may not be very effective (46).

Laboratory Investigations

One of the simplest and easiest test to carry out is the twenty-minute whole blood clotting test. The 20 minute whole-blood-clotting test is done by drawing 2ml of whole blood and putting in a tube made of ordinary glass then observe for clotting after 20 minutes (2).

Haematocrit/ hemoglobin concentration – transient increase indicates an increase in capillary permeability (46).

Platelet count reduces in viper bites (2).

When the white blood cell count is done, neutrophillia with leukocytosis is a common finding. This mostly indicates a sign of envenomation in snake bite victims(40)(54).

Blood film examination and plasma/serum examination should be done to assess for hemolysis (2)

Biochemical abnormalities: elevation in aminotransferases and muscle enzymes is a sign of muscle damage, liver dysfunction leads to elevation of other enzymes, while high levels of bilirubin is an indication of blood extravasation(11).

Other tests include Arterial blood gases/PH, desaturation and Urinalysis(2).

Prevention of Snake Bites

It is advisable to avoid swimming or wading in flood water or swamps to avoid confrontation with sea snakes and other snakes that might have been swept into the water(11).

It is advisable not to drive over snakes, they may get trapped underneath the vehicle and become a source of bites(11).

Wearing shoes – the most venomous snake *Bitis gabonica*, mostly bites below the ankle, wearing boots can prevent envenomation(11).

Catching snakes should also be avoided unless one is trained on how to handle snakes(11).

The inhabitants should avoid sleeping directly on the floor and instead sleep on raised beds, keep doors locked to avoid snakes from creeping into the house in search of rodents like mice and rats (11).

Poultry keeping should not be done in the house. There should be a separate house for poultry to avoid attracting snakes into the house (11).

Clearing the compound of bushes and tall grass and keeping cats are other interventions since domestic cats prey on snakes(29).

Prevalence in Kenya

Mortality from snake bites in rural Kenya is estimated to be 6.7/100,000 per year (36). Ochola et established that in the year 2009, snake bites were responsible for 2.3% mortality in Kenya (36). However, incidences of snake bites are 151/100,000 and only 19% are by potentially venomous snakes(36). When people who are victims of snakebites are shown photographs of several snakes that are locally prevalent, most indicated that they have been bitten by both the venomous and the non-venomous snakes and that the snakes are all capable of causing death when they bite someone(35).

Venomous snakes in Kenya can be broadly classified into two categories for ease of identification of the type of envenoming. The first one is ***Snakes with neurotoxic venom*** – which include Elapids like the Black mamba (*Dendroaspis polylepis*), Jameson's mamba (*D. jamesoni*), the green mamba (*D. angusticeps*), the forest cobra (*N. melanoleuca*) and the Egyptian cobra(*N. haje*) (37,*23*).

Snakes with hemotoxic venom, causing mostly localized effect but can also cause systemic effects – mostly common with the Puff adder (*Bitis arietans*), the black spitting cobra (*Naja nigricollis*), the Gaboon viper (*B. gabonica*), and the red spitting cobra (*N. pallida*), and lastly the saw-scaled viper (*Echis spp*) that is found mostly in Northern Kenya (38,21,36).

Other potentially venomous snakes found in Kenya are the Collubrids which include the boomslang (*Dyspholidus typus*), the vine or twig or tree snake (*Thelotornid kirklandi*) and the well-known burrowing asps (of the genus *Atractaspis*)(39)(40).

Majority of snake bite victims (68%), seek treatment from traditional healers (36). This is the practice in most developing countries inhabited by venomous snakes which makes it challenging to obtain accurate data from incidences of snake bites (41). Therefore most available statistics are based on mere estimates (11).

Only a few studies have been published in Kenya on snake bites and most of them were done more than 10 years ago. In 1992, the highest cases of snake bites were reported in Coast Province at 66 cases, followed by Rift valley at 36 and Eastern at 12 (39, 40, 42)

Conclusion

Literature search for published studies on snakebites in Kenya yield only but a few studies done by Ochola et al, Coombs et al and a few other publications (16,18,39, 53) and Coombs et al did a study in four regions in Kenya in the year 1997 in which Kilifi district was featured, the prevalence of snake bites was found to be the third highest after Samburu and Baringo at 44 per 100,000(18). These studies were limited in scope and did not look into dynamics around management of snake bites in the hospitals in the sampled regions (18). They therefore they revealed little information on the overall picture of snakebite cases in the Coast region. It was necessary to assess the situation once more zeroing in on the largest referral hospital in one of the counties making up the Coastal region. Kilifi County hospital was therefore a strategic facility when it came to studies in this subject area since no study had documented information regarding patterns in management of snake bites at the County hospital.

CHAPTER THREE: MATERIALS AND METHODS

Study Design

This was an exploratory time series descriptive retrospective study in which data from patient files and pharmacy records was abstracted.

The data variables were extracted from patients' files, stock cards and patient registers from January 2013 to December 2016. The researcher extracted the demographic and clinical data from the participants' medical records as retrieved from the archives. The medical records useful in this study also include stock control cards, Kenya Medical Supply Authority (KEMSA) invoices and other relevant records.

Study Site

Kilifi county is in the Coastal Region of Kenya with a total population of 1.2 million people as established by the 2009 population census and covers an area of 12,246² kilometers (61). The total population was projected to reach 1.5 million by 2017 at a population growth rate of 3.1% per annum, it comprises 48% male and 52% female (62). The inhabitants of this county are ravaged by high poverty levels reaching as high as 70%(12). Literacy levels among adults in this county are also low. The main source of income for this population was subsistence farming, tourism and fishing (12).

Kilifi County is administratively divided into seven sub-counties, namely: Malindi, Kaloleni, Magarini, Rabai, Kilifi North, Ganze and Kilifi South. Patients were segregated according to the ward in which they resided.

From the 2016 district health information system 2 (DHIS2) reports, Kilifi County reported the third highest prevalence of snake bite cases after Pokot and Moyale counties(63). This makes this county highly significant in matters snake envenomation.

This county has five level IV hospitals, twenty health centers, 197 dispensaries and 107 private clinics (1). Kilifi County hospital is the largest referral health facility in this vast county with one of the highest workload. It handles referrals from private health care facilities, public health facilities and other hospitals. Snake envenomation was one of the reasons for admission or hospitalization as an in-patient or outpatient at the county referral hospital(40).

With a doctor: population ratio of 1 to 42,625, snake envenomation put the population of Kilifi county at high risk of mortality or debilitating outcomes (64). The hospital has inpatient facilities and more than 120 other public and private facilities refer patients to it. Extraction of data from patient files was conducted at Kilifi County Referral Hospital

Study Period

The study period was four months from March to June 2019. The data collected span five years from 1st January, 2013 to 31st December 2017 focusing on extraction of data from patient files at the County Hospital, the main focus was inpatient records since all snakebite victims were admitted for at least 24 hours, KEMSA delivery notes and stock control cards spanning from 1st January, 2013 to 31st December, 2017. Data collection was done over four months, from March to June 2019.

Study Population

The target population included all patients who were treated for snake bite at the county Hospitals from January 2013 to December 2017.

Eligibility Criteria

Inclusion Criteria

a) All records of patients admitted for treatment of snake bite from January 2003 to Dec 2017

b) All records of patients who had not suffered a snakebite

Exclusion Criteria

a) Patients whose files were missing from the archives

Sample Size Consideration

All snakebite cases from January 2013 to December 2017 were included in the study.

Sampling Method

All identified snake bite cases that fell within the study period were included in the study. Workload data per year was also extracted as a denominator in calculation of incidence rate per annum.

Stock control cards for the pharmacy and all other relevant records in the hospital were also used for data extraction. The relevant records were from January 2013 to December 2017.

All new stock delivery notes from all suppliers who had delivered the drugs of interest, bincards and stock movement records for ASV, hydrocortisone and adrenaline were obtained from the archives for examination.The records were retrieved from the archives, assessed whether the patient was hospitalized for snake bite before being included for data extraction.

3. 8 Data Collection Instruments and Procedures

Data from pharmacy records was extracted in one month using a structured data collection tools (Appendix A). A structured questionnaire was used to extract data from inpatient registers and patient files. The tools were prepared and pretested at the Kilifi County hospital before use and the research assistants were trained on how to use the tools to collect data before pretest and final data collection exercise. Data was collection was done from March to June 2019.

3. 9 Variables

The independent variables included the age, gender, residence, month and time of bite. The dependent variables included the duration of hospitalization, the treatment each individual victim received and clinical outcomes.

Quality Assurance and Data Management

The data collection instruments were pre-tested at the KCH health records department by extracting sample data from identified files and improved appropriately by the researcher. They were also cross-checked by the co-investigator before approval by going through the tools to ensure quality was upheld. The instruments were reviewed by the researcher at the end of each day against the source documents for completeness and accuracy. All the raw data collected was entered into Epi-Info© version 7(2007-2010) software and a database created. The data was backed up on a weekly basis by the researcher. Data cleaning and validation was done before being exported into STATA© (version 13) and R© for analysis.

Statistical Analysis

Quantitative data analysis was conducted using Stata© (Version13). The time series component was analyzed using R©. Descriptive characteristics of the cases was estimated as means, medians, percentage and presented as tables. Prevalence of snake bites was estimated and presented as categories (by type of snake, bite site, residence of the victim). Description of the availability of different treatments was done by percentages of patients per treatment protocol.

Ethical Consideration

Approval for the study was obtained from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UoN-ERC) and Kilifi County Health Research office at the County Health Headquarters. This study was then registered with KNH/UoN-ERC and an official search number obtained (P851/12/2018). Written permission was also obtained from the County, management of the hospital or relevant authorities in order to carry on with the study.

Privacy and confidentiality was of utmost importance to the researcher in order to avoid undue exposure of sensitive patient or hospital information. The data collection tools and patient identity was coded in order to safeguard privacy. A password for the database was generated and put in place to prevent unauthorized access by any other individual apart from the researcher. All the tools that were used in the study were kept under lock and key. The study report and all the material will be finally handed over to the University of Nairobi, School of Pharmacy for storage for five years. An electronic version that was protected by password of the primary data was deposited to the department's e-repository at the University. The researcher will apply to the repository at the end of five years to have the material destroyed.

CHAPTER FOUR: RESULTS

Distribution and Proportion of Snake Bites

The researcher and his associates identified 255 cases of snake bites at the county hospital from 1st January 2013 to 31st December 2017 as shown below:

Table 1: Gender of snakebite victims treated at KCH (2013 to 2017)

Gender	Frequency	%
Male	131	51.4%
Female	110	43.1%
Missing	14	5.5%
Total	**255**	**100.0%**

Male victims were more than female victims comprising of 51.4% while their counterparts were 43.1%. The rest of the victims had their gender missing from the records (5.5%).

The total number of snake bite cases were 255. In 2013 there were 24 cases, 2014 had 12, 2014 was 58, 2016 were 103 and 58 in 2017. There was no death, amputation nor any life altering outcomes in all the cases regardless of whether they got ASV as part of treatment or not. There were only two incidences in which the victims were hospitalized for more than 50 days.

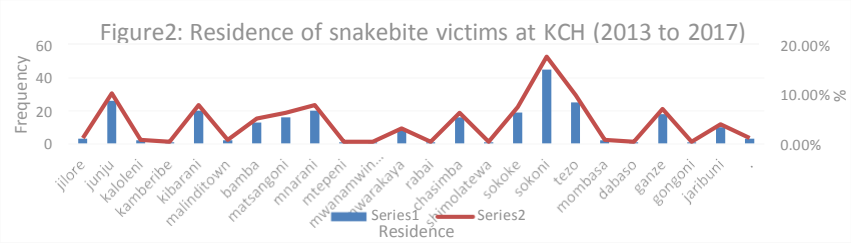

Figure 1:Residences of snakebite victims from January 2013 to December 2019

It is important to note that snake bite victims came from 22 out of 35 wards within Kilifi County while one case was a referral from Mombasa County (Coast General Hospital). These wards are: Jilore, Junju, Kaloleni, Kambe-Ribe, Malindi Town, Bamba, Matsangoni, Mnarani, Mtepeni, Mwanamwinga, Mwarakaya, Rabai, Chasimba, Shimo la tewa, Sokoke, Sokoni, Tezo, Dabaso, Gongoni and Jaribuni wards and that one case from Mombasa County. Most of the victims came from wards closest to the county referral hospital (Sokoni, Tezo, Mnarani, Kibarani, and Sokoke.

Table 2:Residences per ward of snake bite victims per year

Residence	2013	2014	2015	2016	2017	Total
Sokoni	4	4	10	12	10	40
Junju	1	2	4	13	5	25
Tezo	3	1	3	7	9	23
Mnarani	2	0	5	9	3	19
Kibarani	2	1	7	6	3	19
Sokoke	2	0	5	7	3	17
Ganze	0	0	3	8	4	15
Matsangoni	0	1	3	7	3	14
Chasimba	2	0	4	6	3	15
Bamba	0	0	4	6	3	13
Jaribuni	1	2	1	2	1	7
Mwarakaya	0	0	1	0	0	1
Jilore	1	0	0	2	0	3
.	0	1	2	3	1	7
Mombasa	0	0	0	1	1	2
Malindi Town	1	0	0	0	1	2
Kaloleni	0	0	1	1	0	2
Shimo La Tewa	0	0	0	1	0	1
Rabai	0	0	0	0	1	1
Mwanamwinga	0	0	1	0	1	2
Mtepeni	0	0	0	1	0	1
Kambe/Ribe	0	0	0	0	1	1
Gongoni	0	0	0	0	1	1
Dabaso	0	0	1	0	0	1
Total	**19**	**12**	**55**	**92**	**54**	232

While most of the victims had the activity they were doing at the time of bite missing from the file (113, 44.3%), majority were bitten while walking along the pathways (43.9%). A good number were also bitten in their beds while asleep (4.7%), while 9 (3.5%) were bitten while farming and one victim (0.4) was bitten while herding. None of the victims was bitten while swimming.

Table 3: Duration of hospitalization for snake bite victims treated at KCH, 2013 to 2017

Duration Of Hospitalization (Days)	Frequency	%
1	111	45.4%
2	66	27.0%
3	33	13.5%
4	15	6.1%
5	6	2.4%
6	3	1.2%
7	1	0.4%
9	1	0.4%
11	2	0.8%
12	2	0.8%
13	1	0.4%
21	1	0.4%
27	1	0.4%
63	1	0.4%
77	1	0.4%
Total	**245**	**100.0%**

Range is 1 to 77 days of admission, with a mode of 1 day. However, on average, the patients spent 3 days in the hospital while admitted for management of snake bite.

From the 255 cases, 49 were referred to Kilifi County Hospital from the following areas:

Table 4:Origin of Snake bite cases referred to KCH 2013 to 2017

Residence	Frequency	%
Junju	13	26.5%
Kibarani	2	4.1%
Bamba	4	8.2%
Matsangoni	2	4.1%
Mnarani	3	6.1%
Mtepeni	1	2.0%
Mwarakaya	2	4.1%
Chasimba	3	6.1%
Shimolatewa	1	2.0%
Sokoke	3	6.1%
Sokoni	1	2.0%
Tezo	5	10.2%
Mombasa	1	2.0%
Ganze	8	16.3%
Total	**49**	**100.00%**

There were a total of 17 health facilities that referred patients to KCH for snake bite treatment within the study period:

Vipingo HC

Dida disp

Mavueni HC

Medical Center

Jaribuni disp

Chumani HC

Coast Gen Hospital

Private Clinic

Dispensary

Kanamai HC

Ngerenya Disp

Tezo Commmunity Hosp

Mtondia Disp

Chasimba HC

Mephi medical health

Bamba HC

Vitengeni HC

Ganze HC

Matsangoni Disp

Palakumi Disp

Health Centers were responsible for 68.3% of snake bite cases referred to KCH while dispensaries referred 29.3%. One case came from Coast General Provincial Hospital in Mombasa (see table in Appendix 4)

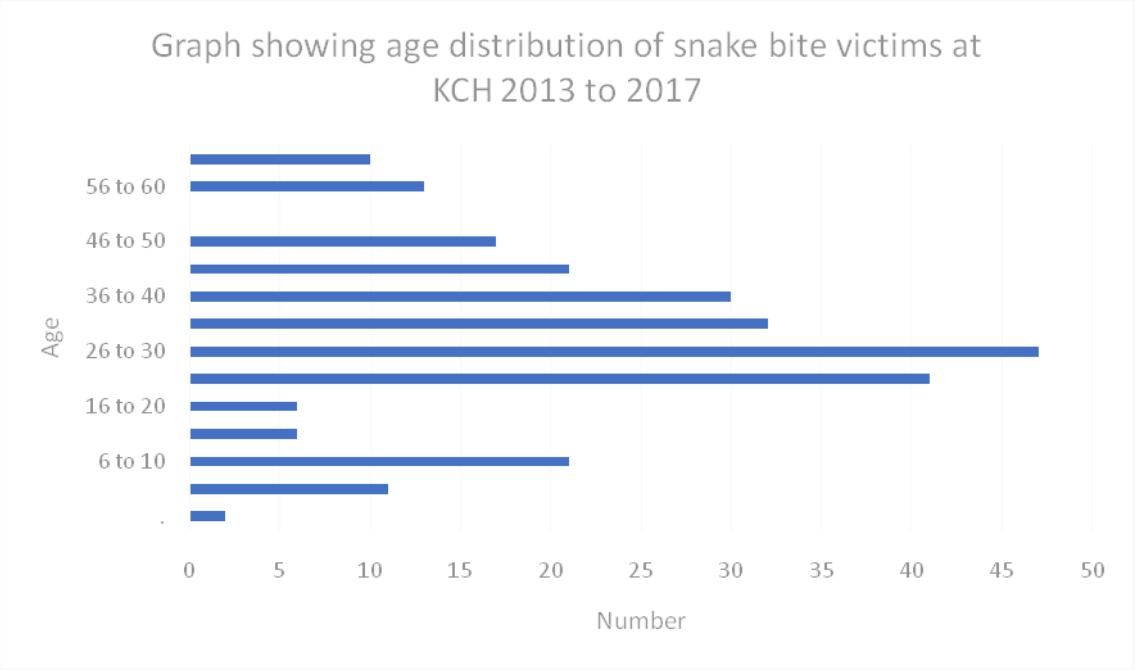

Figure 2:Age distribution of snake bite victims at KCH 2013 to 2017

Majority of the victims were between 15 to 40 years of age. Majority of the patients take more than 2 hours to reach the facility after being bitten by a snake as shown below:

Table 5: Time of arrival and treatment with ASV at KCH for snake bite victims, 2013 to 2017

Time	Frequency	Number treated with ASV	% that received ASV
< 30 minutes	10	1	10.0%
30 min to 1 hour	11	5	45.5%
1 - 2 hours	28	2	7.1%
> 2 hours	96	17	17.7%
Total	**145**	**25**	**17.2%**

The patients who arrived at different time intervals and whether they received ASV, the table above summarizes the findings.

The table below summarizes age of snake bite victims treated at Kilifi County Hospital from 2013 to 3017

Table 6:Summary of age of snake bite victims treated at KCH, 2013 to 2014

Age (yrs)	Frequency	%
<5	11	4.3%
5 to 10	21	8.2%
11 to 15	6	2.4%
16 to 20	6	2.4%
21 to 25	41	16.1%
26 t0 30	47	18.4%
31 to 35	32	12.5%
36 to 40	30	11.8%
41 to 45	21	8.2%
46 to 50	17	6.7%
51 to 55	0	0.0%
56 to 60	13	5.1%
61+	10	3.9%
Total	**255**	**100.0%**

The most affected age set was between 21 to 30 years of age. This is also confirmed in figure 2 below.

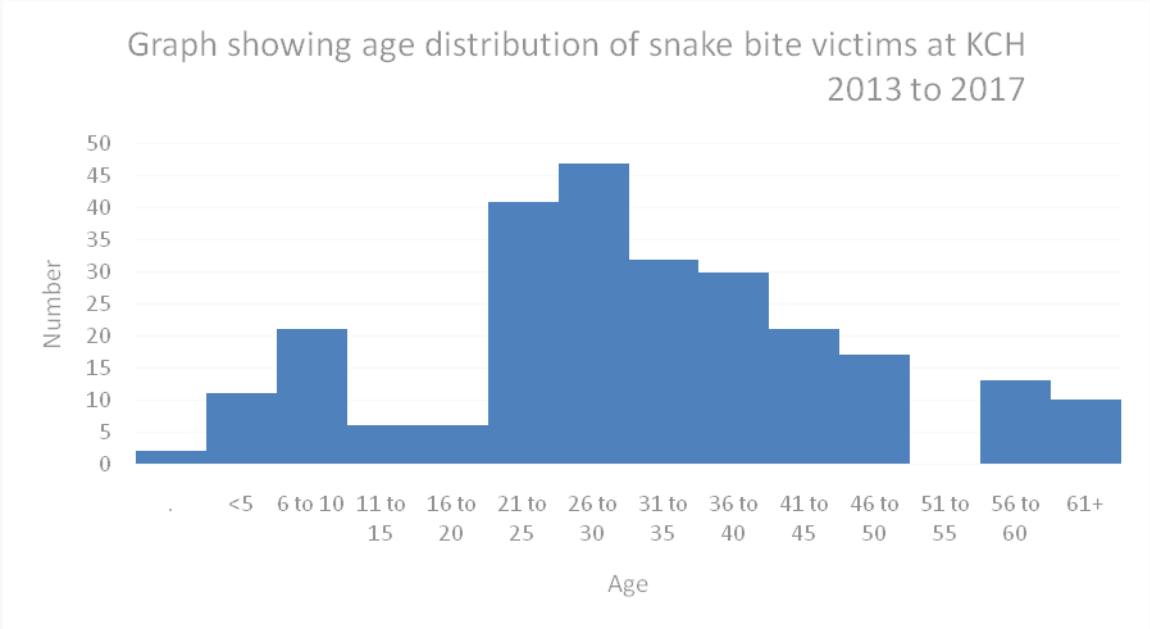

Figure 3: Age distribution of snake bite victims at KCH, 2013 to 2017

The table 8 below summarizes the number of incidences per age set and gender. Putting gender into consideration; males of age between 16 to 20 years are most affected (9.4%) while for females, those of 11 to 15 years are most affected by snake bites (8.6%). There was however no case of snake bite reported in either gender in the 51 to 55 age sets. It is also important to note that males of +61 years of age still reported a number of cases accounting for 3.7% of reported incidences among male while their female counterparts had no reported case.

Table 7:Age set and gender of snake bite victims at KCH, 2013 to 2017

Age	Male		Female		Total
	Frequency	% of total No. of cases	Frequency	% of total No. of cases	
<5	8	3.3%	3	1.2%	11
5 to 10	12	4.9%	8	3.3%	20
11 to 15	19	7.8%	21	8.6%	40
16 to 20	23	9.4%	17	7.0%	40
21 to 25	18	7.4%	12	4.9%	30
26 t0 30	15	6.2%	14	5.7%	29
31 to 35	6	2.5%	12	4.9%	18
36 to 40	7	2.9%	10	4.1%	17
41 to 45	7	2.9%	6	2.5%	13
46 to 50	9	3.7%	1	0.4%	10
51 to 55	0	0.0%	0	0.0%	0
56 to 60	3	1.2%	3	1.2%	6
61+	9	3.7%	1	0.4%	10
total	**136**	**55.7%**	**108**	**44.3%**	**244**

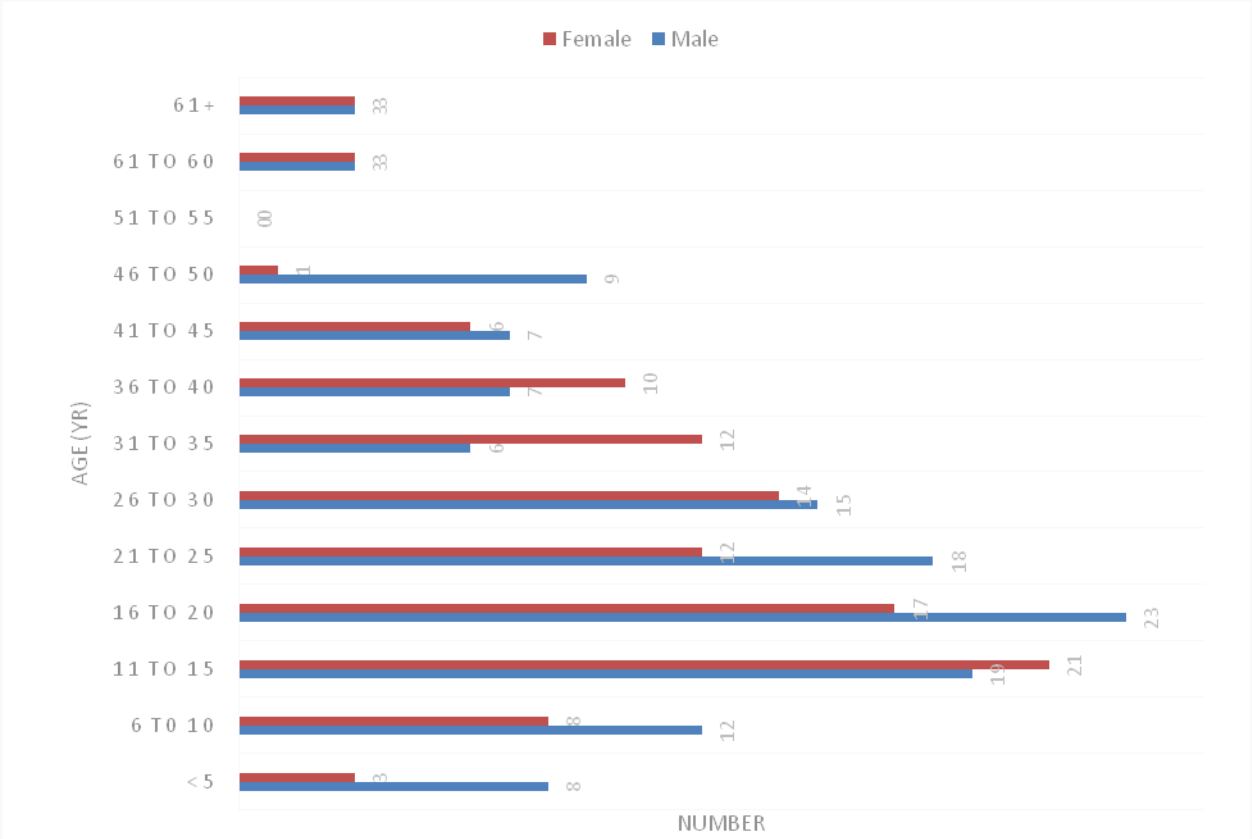

Table 8: Distribution of age by gender of snakebite victims at KCH, 2013 to 2017

Table showing proportion of snake bite cases at KCH from 2013 to 2017

Table 9:Proportion of snake bites by inpatient workload at KCH, 2013 to 2017

	Kilifi County Hospital			
Period / Data	**Inpatient Admissions Over Five**	**Inpatient Admissions Under Five**	**Snakebite cases**	**Proportion per 1,000 Admissions**
2013	9,005	-	24	3
2014	12,164	-	12	1
2015	12,529	-	58	5
2016	9,455	2,428	103	9
2017	4,958	2,112	58	8
TOTAL	**48,111**	**4,540**	**255**	**5**

On average, snake bites were responsible for 5 in 1,000 admissions at the hospital. The highest incidence proportion was 9/1,000 admissions in the year 2016. The trend in snake bite cases has been an increasing one.

Supply Situation of ASV, Hydrocortisone and Adrenaline

From pharmacy records, ASV, Adrenaline and Hydrcortisone injection were all available during the study period. However, out of the 255 snake bite cases, none received Adrenaline injection nor any blood transfusion while 55.7% were treated with Hydrocortisone injection. 63.53 of the snake bite cases got Nonsteroidal anti-inflammatory agents (NSAIDs) as part of their treatment. Only 48 (19%) of the victims received antisnake venom (ASV), while 146 (47.2%) received antitetanus toxoid.

Table 10: Percentage of snake bite patients that received NSAIDs and other treatments at KCH from 2013 to 2017

Treatment	Frequency	% n=255
Antibiotic	181	71.0%
TT	146	57.3%
Paracetamol	160	62.8%
Paracetamol and NSAID	12	4.7%
NSAID	161	63.1%
Antihistamine	48	18.8%
hydrocortisone inj	142	55.7%
ASV	48	19.0%
Opioids	1	0.4%

It is also worth noting that 71.0% and 63.1% of the snakebite victims received antibiotics and NSAIDs respectively as part of their treatment. Use of NSAIDs is contraindicated in snake envenomation due to the risk of exacerbating bleeding in cases where the victim suffered a bite by a snake with hemotoxic venom like the adders.

Sokoni, Junju and Tezo wards had the highest incidences respectively and accounted for 37.7% of all the treated snake bite cases for the study period - with Sokoni having the highest number.

Seasonal Variability in Snake Bites

Test for seasonality was done using R© software as shown in a series of diagrams below. The ACF plot showed strong positive correlation with a trend that was increasing monthly. The same is also confirmed by the box plot. The trend was assessed using moving average method after decomposition of the data. Interrupted time series analysis show that the events of snake bites increased from October 2014. This shift was statistically significant since the P-value was below 0.05. For time interval, the monthly change in snake bites was approximately one bite per month (Pvalue below 0.05). The pattern of change was best modelled using a quadratic equation. Snakebite cases peaked in June and December of every year.

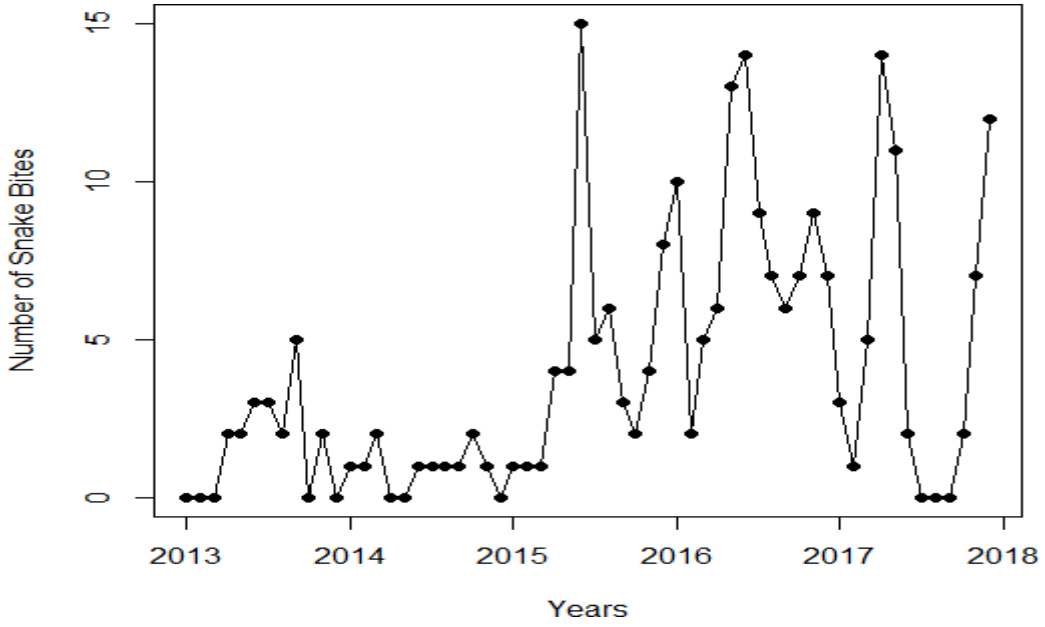

Figure 4: Time series plot of snakebite cases at KCH, 2013 to 2017

The box plot below confirms the seasonality of snake bite cases as depicted above in the time series plot. There was a clear upsurge in cases at mid - year (June) and also at the end of the year in December

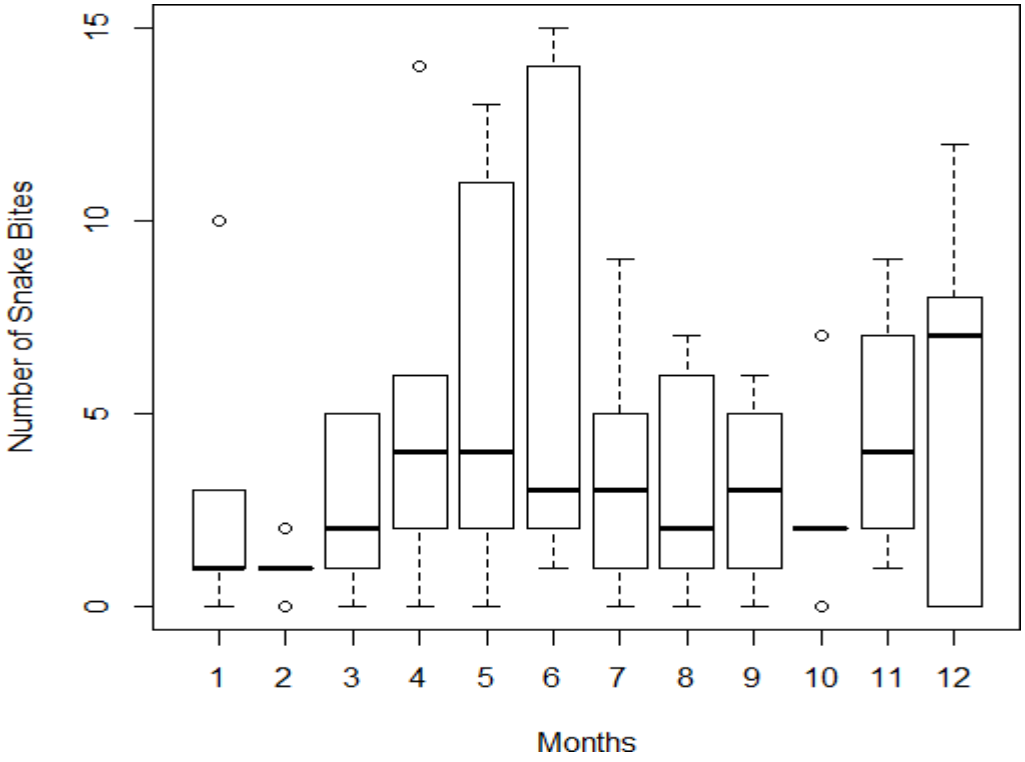

Figure 5:Box plot showing snake bite cases at KCH

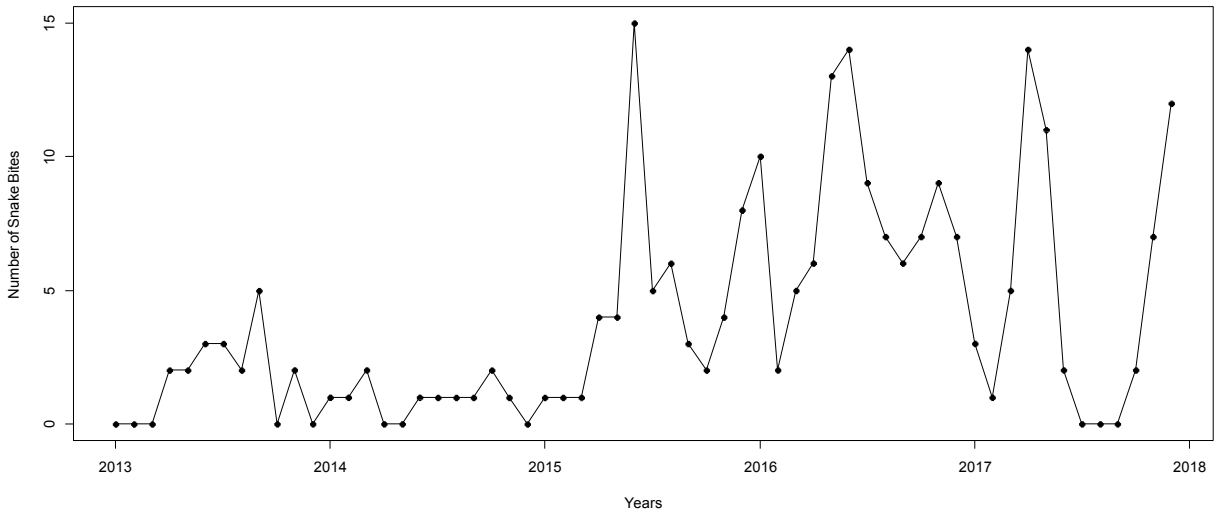

Figure 6:Decomposed plot showing snakebite cases at KCH

The trend was increasing with time while there is a clear upsurge in cases in June and December of every year.

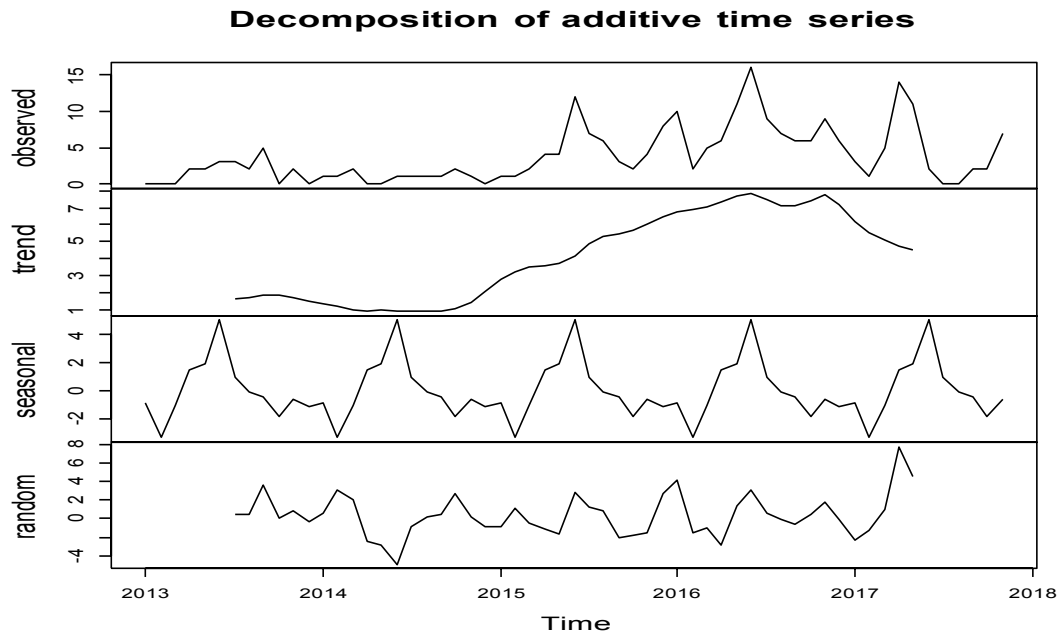

Figure 7:Showing trend, random effect and seasonality of snake bite cases

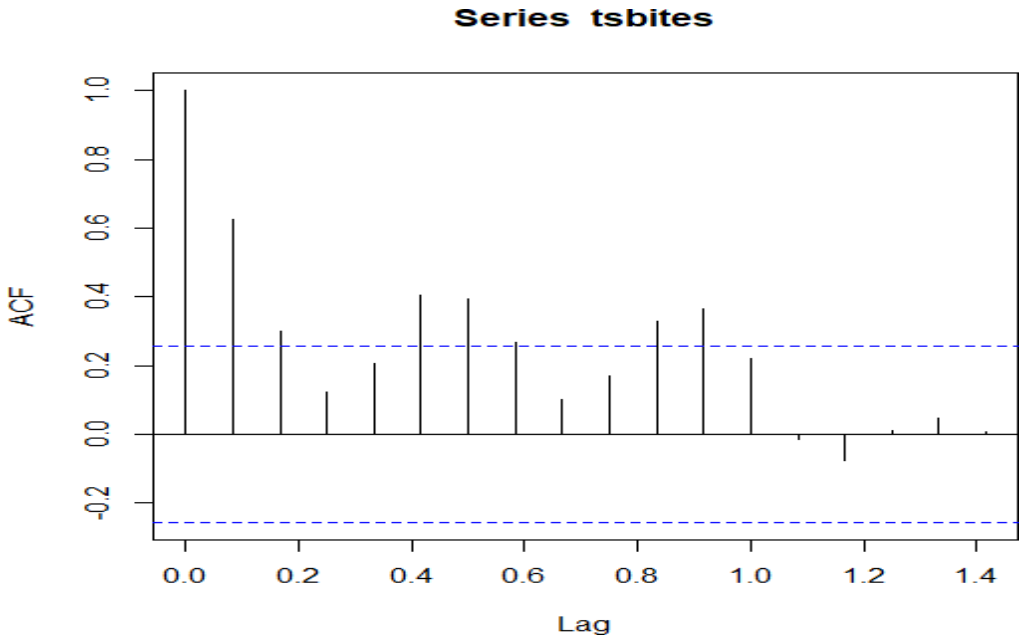

Figure 8: Residuals in Time series analysis of snake bite cases at KCH

The figure above shows the residuals in time series analysis which depicts a clear random effect in the incidences of snake bites at KCH.

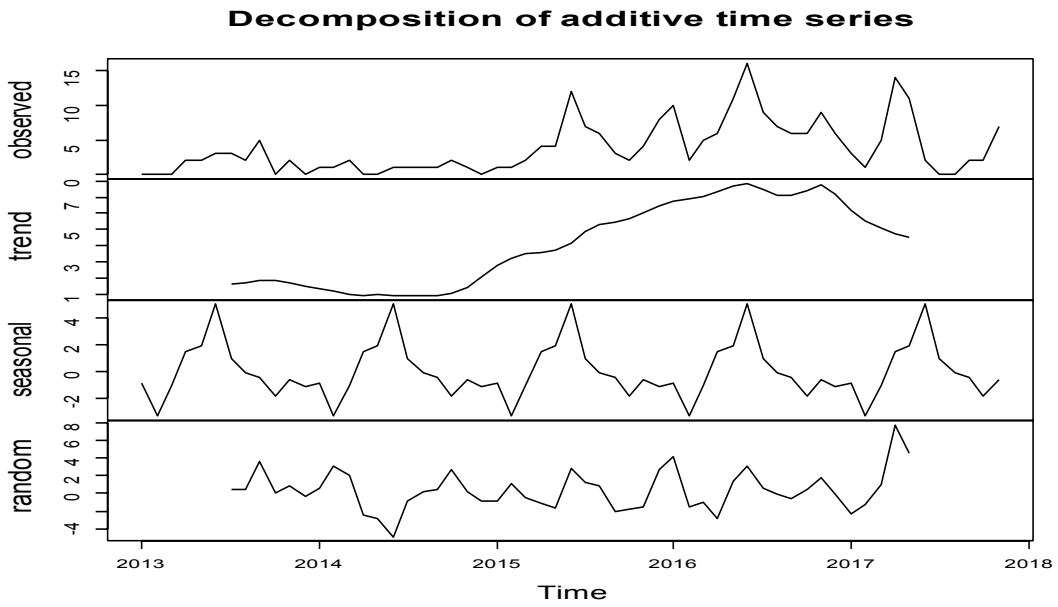

Figure 9: Decomposed plot showing the trend, seasonality and randomness of snake bite cases at KCH

The figure below shows the five year forecast of treated snake bite cases at Kilifi County Hospital from January 2018 to December 2022. With an increasing trend, the snake bite cases are projected to rise to about 318 per annum by end of the year 2022.

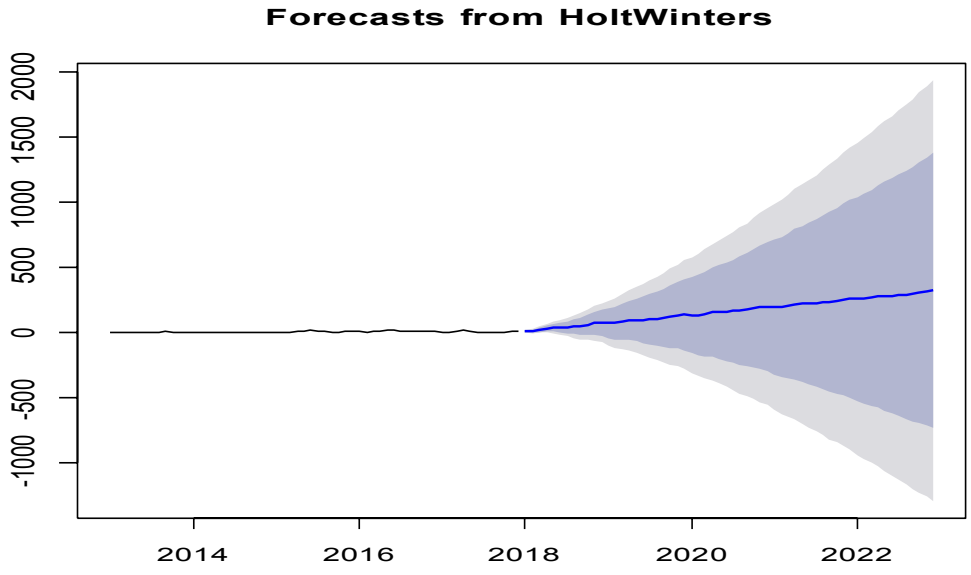

Figure 10:Five year forecast of snakebite cases at KCH from 2018 to 2022

Available anti-snake venoms

The county hospital receives anti-snake venom from two sources: one from the government agency (Kenya Medical Supplies Agency (KEMSA)) and another one from a private entity called Bioken Kenya Situated in Watamu. All the antivenoms were polyvalent.

Figure 11:Vial of Antisnake venom from Bioken, Watamu, obtained at KCH in June 2019

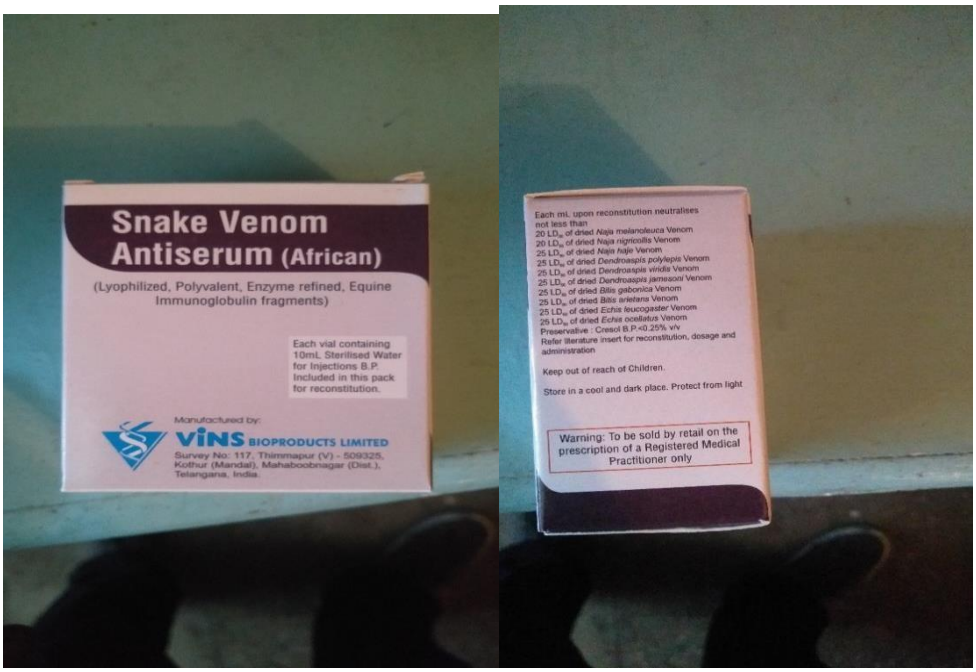

Figure 12:Anti-snake Venom supplied by KEMSA obtained from KCH Pharmacy in June 2019

Table 11: Summary signs and symptoms as extracted from files of Snake bite victims at KCH from 2013 to 2017

	Description	Frequency	%
Syndrome 1	Presents as localized envenoming with bleeding/clotting disturbance. This is common in all Viperidaes	189	73.5
Syndrome 2	Includes local envenoming that result into bleeding, followed by shock, and acute renal damage. This occurs commonly in bites by Russell's Viper (which is also known as the hump-nosed viper) that is found in Sri Lanka and South-Western India (31). Another symptom is occurrence of conjunctival edema sometimes accompanied by acute pituitary insufficiency. This is typical in envenoming by Russell's viper found mostly in Myanmar	0	0.0%
Syndrome 3	Commonly present as swelling accompanied by paralysis. This is common in cobra and mamba envenoming	21	6.2%
Syndrome 4	Includes paralysis with minimal local swelling. If the victim was bitten on land the snake might be a krait bite, but if the occurred in the Ocean, estuary or water body, it is most likely due to sea snake envenoming	2	0.8%
Syndrome 5	Occur as paralysis with an acute renal injury characterized by dark brown urine common with Russell's viper, krait or sea snake envenomation	0	0

From the tabulation above, most of the snake bites (73.5%) are most likely due to envenomation from vipers while 6.2% are due to mambas and cobras.

CHAPTER FIVE: DISCUSSION OF RESULTS

5.1 Discussion

Majority of the snake bite victims were residents of Kilifi County and most of them came from Sokoni ward (18.1%). This was most probably due to the proximity of the county hospital to this area and the ease of transporting the patients to this facility. Junju Ward was the source of highest number of snake bite cases referred to this hospital (26.5%) while Vipingo health center was the source of most referrals at 27.9%. Therefore focusing on the areas around Vipingo Health Center, Junju, Sokoni, Tezo, Mnarani and Kibarani wards in efforts to prevent snake bites may lead to reduction in these incidences by more than 50.0%. This is in sync with the findings from literature review where Kilifi was identified as one of the areas with high incidences of Snake bites (40). In India, where there are also high incidences of snakebites, rural areas have a higher incidence ratio of snake bites than urban areas, at a ratio of 1:4.7 which shows that snake bites affect rural folks more, like residents of Kilifi, than those in urban dwellings (31).

At below 10 years of age, males are more likely to get bitten while females are more in the 30 to 40 year age group. However, the incidence of snake bites was equally distributed in either gender in most of the age clusters. This may have been due to level of activity, with young boys engaging in errands that involve taking walks along the paths more often and also mothers in their late 20s and early 30s. Other studies in Kenya also established that majority of snake bite victims were below 15 years of age (39).

Walking along pathways was associated with high number of snake bite cases at 43.9% (112). Of all the cases having reported being bitten along the way, 4.7% and 3.5% were bitten while sleeping and farming respectively. Therefore, making the pathways safer by widening them through clearing of bushes along the footpaths or any other initiative might significantly reduce the number of snake bites. The number two place where the victims were most likely to be bitten was at home while they were asleep. The snakes might have crawled into the houses in pursuit of rodents, water, chicken or shelter(58). Having measures to reduce possibility of having snakes crawl into houses would therefore have led to fewer cases of bites being reported.

Measures like having beds raised above the floor, having tighter doors and windows and making walls of homesteads devoid of holes through which the snakes can crawl into the houses can be helpful in preventing snakebites. Control of rodents and avoiding sharing houses with livestock can also form one of the strategies of reducing snake bites since snakes

are known to hunt for birds and their eggs as food. Wearing protective gear like boots or shoes can also form a bigger part of public health strategy to reduce incidences of snake bites while farming. This is also advocated for in the WHO's *Guidelines for Prevention and Management of Snake Bites in Africa*(66).

Snake bites accounted for 5 per 1,000 admissions annually with a range of 1 to 77 days of hospitalization as shown in table 8. Similar findings were also noted in Zimbabwe where morbidity was minimal with mortality of less than 0.4% of the 250 cases admitted (48). Although few in number, these cases have a higher chance of raising bed occupancy in a referral hospital therefore resulting into high cost of care for the community due to prolonged admission(25). This, coupled with lost productivity, can lead to a rise in poverty level since a large proportion of victims are from the productive age group(14). Farming, being the main activity that employs majority of the inhabitants of this country, was also the third highest source of exposure to snakebites during the study period(14). Strategies that can make farming safer can also be of great value in reducing incidences of snake bites. Wearing boots while farming, mechanization of farming and rodent control can form part of snake bite preventive strategy. Similar advice is also documented by other researchers who established that populations in Sub-Saharan Africa are more at risk of snake bites due to sharing habitat with the reptiles(23).

Regarding management of snake envenomation, 70.98% of all the cases were put on antibiotics as a part of treatment while only 19% received anti-snake venom, as shown in table 9. 47% of the victims received tetanus toxoid injection while 63.14% received NSAIDs as part of treatment. The international guidelines on treatment of snakebites from WHO advocates for use of antibiotics as a prophylaxis against a possible secondary bacterial infection. However, his practice should be implemented with caution to avoid unnecessary misuse of these drugs which can easily lead to life threatening side effects, antibiotic resistance and a high pill burden. The county referral hospital was doing a great job in following these guidelines. In Kwa Zulu Natal where 363 records of snake bite victims were examined, there was minimal link between clinical outcome in the victims and antibiotic use (67). This study (Kwa Zulu Natal) advocates for use of antibiotics only in cases with sepsis(37). The rest of the treatments are in order apart from use of diclofenac, ibuprofen and other Non-steroidal anti-inflammatory inhibitors (NSAIDs) in management of pain. Other authors also discourages use of NSAIDS in cases of snakebites in Emergency Treatment of Snake bites (55). In case where a victim has been bitten by a snake, chances of exacerbating bleeding is raised when NSAIDs are administered to the patient(52). Envenomation by a

snake that has hemotoxic venom and subsequent administration of NSAIDs to the same victim is discouraged due to the risk of exacerbating bleeding due to inhibition of blood clotting (51). The drug recommended for management of mild pain in snake bite victims is Paracetamol, which was prescribed in 62% of the victims. In cases with severe pain, the clinician is advised to explore use of opioids as an alternative option which was observed in only one patient that was treated for snake envenomation at Kilifi County Hospital during the study period (50).

Although the hospital had anti-snake venom in stock, only 19% of snake bite victims received this definitive treatment. The utilization of this medicine is low given that some of the cases that were not offered this treatment had syndrome 1 and 3 symptoms of snake envenomation. Sensitizing clinicians on use of ASV in treatment of snakebites might be of help to avoid under-treatment of victims in cases that exhibit clear signs of envenomation. In South EastAsia, expertsadvocate for more prudent us of ASV in cases with clear signs and symptoms of envenoming (53).

However, the clinician should always be on the lookout for signs and symptoms of anaphylaxis which can easily lead to shock and eventual death of the patient. It's advocated that a vial of adrenaline is made available at hand before a patient receives ASV in order to combat anaphylaxis immediately it happens(54). Proper use of ASV can significantly reduce the duration of hospitalization for the victims since its known to enhance recovery and leads to better clinical outcomes(47).

There was only one case that had adverse outcome that required amputation of the right leg, a procedure which was subsequently declined by the patient. It is important to note that the same patient who declined amputation went on to make a complete recovery from this experience. This shows that although snakebites are potentially fatal, the rate of fatality is extremely low (37).

The study established that snake bite cases were highest in the months of June and December each year. This coincides with the dry season of the year just as picked out by Snake bite management experts in their assessment of snakebites at Triangle Hospital, Zimbabwe(68,69). There was also a strong seasonal variation and a clear trend showing that every year, there was a reduction in snake bite cases treated at KCH in the months of April and September. The cases peaked as one heads towards December, then started declining from January and peak again in June. It will therefore be important to plan to have higher stocks of antivenom during the peak period in order to avoid expiries of the expensive ASV.

The community can also be sensitized to be cautious during this period by avoiding unnecessary exposure to snake bites(66).

This exposure can be mitigated by keeping compounds clean, free of bushes and overgrown grass, wearing protective shoes while working in the farms and when taking a walk along the paths, rodent control, improvement in housing to avoid snakes crawling into living spaces and avoiding sharing houses with livestock, especially birds (66). Ultimately, being careful and watchful at a personal level can be of value in avoiding exposure to snake bites(51).

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

Conclusions

The study found that male children below the age of 15 and mothers between 20 to 30 years of age were more at risk of snake bites. Out of the 255 cases of snake bite that were treated in the hospital from 2012 to 2017, only 19.0% received ASV despite the fact that the hospital always had the medicament in stock. It is also notable that there were no mortalities from snakebite cases.

Recommendations

Recommendations For Policy Changes

Given the low prevalence of snake envenomation amidst scarcity of resources and the costly nature of ASV, it will be of utmost importance that the county hospital consider seasonal variability of snake bite cases in supply planning for anti-snake venom to avoid unnecessary wastage. It will also be prudent to increase uptake of ASV by sensitizing clinicians on proper management of snake envenomation. Patients who exhibit clear sign of envenomation should all be put on ASV to improve their recovery unless there is a clear contraindication. Health workers from facilities that refer large number of snake bite victims to KCH should also be trained and supplied with the ASV. Physicians, clinicians, nurses and all other health workers involved in treatment of snakebite cases should be trained on need to avoid NSAIDs in these cases.

The community ought to be sensitized on how to minimize exposure to snake bites through cleaning of compounds, clearing of bushes along pathways, proper animal husbandry that does not involve sharing houses with livestock, and use of protective gear in the farms. The study recommends a more community-based approach which will unveil incidence rates for majority of snake bite cases that are managed at home and never get to the hospital in order to generate a wholesome picture of the snake envenomation problem.

Recommendations for Further Research

Due to funding challenges, the focus group discussions that were to be done as part of the study were not conducted. Therefore, we could not establish the community dynamics that are put at play when one of the community members is bitten by a snake. We were not also able to identify types of snakes that were implicated in the numerous cases since this information was missing from the patient files. The syndromic approach was utilized to classify the observed signs and symptoms using the WHO scale of syndrome 1 to 5 (20).

The study could not evaluate the effectiveness of the available ASVs due to the small sample number of victims identified at the county hospital. Other areas that were not covered include: evaluation of the effectiveness of available anti-snake venoms and assessment of supply chain data. We also recommend a scale up of the study to cover all the major hospitals, both private and public, to unravel the true burden of snake envenomation in the county. It will also be prudent to conduct a study to assess the efficacy of the supplied anti-snake venoms in the market to generate facts on this subject.

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BUDGET

COMPONENT	UNIT OF MEASURE	DURATION/Number of days	COST (Kshs)	TOTAL (Kshs)
PERSONNEL				
Research assistant	5pax	60	1500	**450,000**
Data Analyst				**60,000**
Training and pretesting of tools	10 pax	2	7000	**140,000**
STATIONERY & SUPPLIES				
Printing-consent form	1 copy	3 pages	10	**30**
-Data collection tool – from patient registers	250 copies	9 pages	10	**22,500**
-Final report	1 copy	150 pages	10	**1500**
photocopying-consent form for hospital and county	2copies	10pages	3	**300**
-Data collection tool - pharmacy	369 copies	3 pages	3	**3,321**
-final report	5 copies	90 pages	3	**1,350**
Binding	6 copies	1	500	**3,000**
SERVICES				
ERC fees		1		**2,000**
				684,001

WORKPLAN

Research activity	July 2018	Oct 2018	Nov 2018	Dec 2018	Jan 2019	Feb 2019	Mar 2019	Apr 2019	May 2019	Jun 2019	July 2019	Aug 2019
Proposal development and writing												
Ethical review												
Pilot study												
Data collection												
Data analysis												
Report writing												
Submission of final thesis												
Thesis defense												
Dissemination												

APPENDICES

Appendix I: Data Collection Tool

Data collection tool – from patient files and inpatient registers

(These are the agreed variables .Any other input is welcome.)

OP/IP number _____

Age (years) _____

Biodata

Sex	Male		Female	Other
Date of admission			Time	
Time of bite	Date		Time (hr)	
Referral (Tick appropriately)	Yes		No	
Name of referring facility			County	Level (I,II,III,IV,V)
Residence of victim (ward) –Tick appropriately	Adu			
	Bamba			
	Chasimba			
	Dabaso			
	Ganda			
	Ganze			
	Garashi			
	Gongoni			
	Jaribuni			
	Jilore			
	Junju			
	Kakuyuni			
	Kaloleni			
	Kambe/Ribe Kayafungo			
	Kibarani			
	Magarini			
	Malindi town			
	Marafa			
	Mariakani			

	Matsangoni				
	Mnarani				
	Mtepeni				
	Mwanamwinga				
	Mwarakaya				
	Mwawesa				
	Rabai				
	Ruruma				
	Sabaki				
	Shella				
	Shimo la tewa				
	Sosoke				
	Sokoni				
	Tezo				
	Watamu				
	Taita Taveta				
	Mombasa				
	Tana River				
	Lamu				
	Kwale				
	Other (give name)				
Duration of admission(days)					
Activity at time of bite (Tick appropriately)	Herding		Presentation of patient at admission	***Tick appropriately***	
	farming			Prostration	
	Walking to work, water point, market etc			Profuse bleeding	
				Intense pain with swelling	
	swimming			paralysis	
				Tingling sensation	
	Asleep			hysterical	
	other			Other (specify)	

Clinical information

Anti-venom given or not and also assess whether any other treatments was given

drug		Tick appropriately	
		Yes	No
ASV			
	Type of ASV	Monovalent	Polyvalent
Corticosteroid (hydrocortisone inj)			
antihistamine			
paracetamol			
NSAIDs			
Anti-Tetanus toxoid			
antibiotic			
Adrenaline			
Blood transfusion			
Other (specify)			

Referred to another facility Y/N

reason for referral eg lack of treatment options or expertise? Lack of drugs, antivenom

Reason fo referring from Kilifi County Hospital to other facility	
Lack of appropriate medical infrastructure	
Lack of ASV	
Inadequate skills	
other	

Outcome of patient on discharge (Dead/Alive)

Amputation	leg	left	***Outcome***	Yes	no
			Vision impairment		
		right	contractures		
	arm	left	paralysis		
		right	Hypo-pituitary		
	Finger(s)		Dead		
			Renal impairment		
	Toe(s)		Other(specify)		

Appendix II: Snake Envenomation Indicator Definition and Interpretation

INDICATOR	DEFINITION	CALCULATION	INSTRUMENT
1. Annual ratio of patients hospitalized with snake bite per 100,000	-This is a measure of incidences of snakebite cases in the wards. -Provides information on snake bite incidences.	-Divide the number of patients admitted with a snake bite per annum by the total number of patients admitted that year and multiply by 100	Epinfo© spreadsheet
2. Annual percentage of snake bite victims who got ASV	- To measure the average number of patients with snake bite who got ASV -The aim is to determine the extent ASV use in management of snake envenomation.	-Divide the total number of patients who received ASV with the total number of snake bite cases annually.	Epinfo© spreadsheet
3. Percentage of snake bite victims who got appropriate supportive treatment	-This measures the degree of patients with snake bite who appropriately managed	-Divide the number of snake bite cases who are appropriately managed divide by all patients with snakebite and multiply by 100	Epinfo© spreadsheet
4. The average duration of hospitalization due to snake bite.	-This indicator measures the days that the patients are hospitalized due to snake bite.	-	Epinfo© spreadsheet

Appendix III: Approval to Conduct Study in KCH

COUNTY GOVERNMENT OF KILIFI

DEPARTMENT OF HEALTH SERVICES

When Replying quote
Email; chmtkilifi@gmail.com
REF: HP/KCHS/VOL.X/211

P. O. Box 9-80108
Kilifi
Date 16th April 2019

OFFICE OF THE COUNTY DIRECTOR

Dr. Mang'ong'o David Olungo,
Dept. of Pharmacology and Pharmacognosy
School of Pharmacy
University of Nairobi,
Reg No: U51/7577/2017
Nairobi, Kenya

Dr. Mang'ong'o

RE: DEPARTMENTAL AUTHORIZATION TO CARRY OUT A STUDY IN KCH

The Kilifi County Department of Health Services is in receipt of your request to conduct a study titled, ***"Evaluation of Impact of Supply Chain of anti-snake venom and related drugs on management of snakebites at Kilifi County Referral Hospital",*** that received ethical approvals from **KNH-UoN ERC** ***Ref: KNH-ERC/A/90***.

The Department is glad to grant you authorization to conduct your study over a period of one year (March 2019-March 2020) in **Kilifi County Hospital** in line with the approved study protocol. It is required that you engage the facility administration where you will be conducting the study prior data collection.

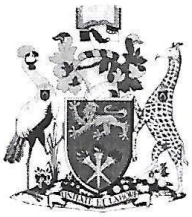
Upon completion of the study, you are required to share your findings, and recommendations with the Department of Health Services, Kilifi County.
Sincerely,

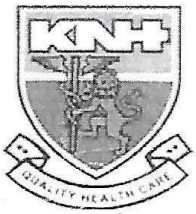
COUNTY DIRECTOR OF HEALTH
KILIFI COUNTY
16 APR 2019
P. O. Box 9 - 80108, KILIFI

Vincent Iduri
Ag. Director of Health
KILIFI COUNTY

Cc:
CEC – Health Services, Kilifi County
Chief Officer of Health, Kilifi County
Chief Officer Public Health, Kilifi County

Appendix IV: KNH/UON-ERC Letter of Approval





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KNH-UON ERC
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Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/90

14th March, 2019

Mang'ong'o David Olungo
Reg. No.U51/7577/2017
Dept.of Pharmacology and Pharmacognosy
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear David

RESEARCH PROPOSAL: EVALUATION OF THE IMPACT OF SUPPLY CHAIN OF ANTI-SNAKE VENOM AND RELATED DRUGS ON MANAGEMENT OF SNAKE BITES AT KILIFI COUNTY HOSPITAL (P851/12/2018)

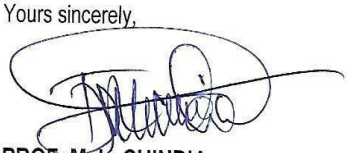
This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 14th March 2019 – 13th March 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,



PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Pharmacy, UoN
The Chair, Dept. of Pharmacology and Pharmacognosy, UON
Supervisors: Dr. Kipruto Arap Sinei, Dr. Sylvia A. Opanga
Collaborator: Mrs. Eveline Langat, (Kilifi County Health Management Team)

Appendix V: Certificate of Plagiarism

18/11/2021

18/11/2021

Factors That Influence Clinical Outcomes of Snake Bites With Special Reference To Supply of Anti-Snake Venom and Related Drugs At Kilifi County Referal Hospital In Coastal Kenya

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