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Original Article

Snake Bite: Patterns, Management and Out-Come in Muzaffarabad, Azad Jammu & Kashmir

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ABSTRACT

Background: Annual death rate attributed to snake bite accounts for 1.9 per 100,000 population in Pakistan. Southern parts of the country are affected the most; data is scarce from northern parts.

Objectives: To study the patterns of snake bite, clinical features, management approach and out-come in Muzaffarabad, Azad Jammu & Kashmir (AJK).

Methods: This was a descriptive observational study conducted from June 2017 to December 2018 at the Department of Internal Medicine, Sheikh Khalifa Bin Zayed Al Nahyan Hospital, Muzaffarabad, Azad Jammu & Kashmir. A detailed demographic and bite inquiry followed by thorough clinical examination was documented for each patient. This was followed by laboratory investigations including urinalysis, complete blood count, coagulation profile, renal function tests and ECG. Polyvalent snake Anti-venom as well as other supportive treatment was administered according to World Health Organization guidelines.

Results: Out of 79 patients, 49 (62%) were females and 30 (38%) were males. Mean age was 33 years (SD±11.88). Fang marks were seen in 67 (84.8%). 48 patients (60.8%) were bitten between dusk to sunrise. Bite was on lower limb in 61 (77.2%) and upper limb in 16 (20.3 %). 75 (94.93%) had features of hemotoxic or cytotoxic envenomation comprising; local swelling or vesicles in 42 (53.1%), hypotension in 19(24.1%), epistaxis and hematuria in 11 (13.9%) and 16 (20.3%) respectively, prolonged prothrombin time and APTT in 41(51.9%) and 44 (55.7%) respectively. Raised serum creatinine and urea were observed in 52(65.8%) and 5 (6.3%) respectively. Symptoms of neurotoxicity were observed in 4(5.05%) patients. 2.5% (n=2) patients were placed on mechanical ventilator. 2.5% (n=2) patients did not survive the massive hemorrhagic diathesis.

Conclusion: High incidence of hemotoxic and cytotoxic envenoming have been reported in district Muzaffarabad. Complete recovery is attributed to prompt general supportive treatment and specific treatment with antivenin therapy.

Key words: Snake Bites, Snake Venoms, Muzaffarabad, Kashmir

Background

Most snake bites are not lethal to humans. However, venomous snake bites can be fatal if not treated promptly. Global incidence of venomous snake bite is around 2.5 million per year, with consequent more than 100,000 deaths.[1] In the United States 4000 to 7000 snake bites are reported annually. Out of these reported incidents, almost 2000 are caused by venomous snakes.[2] Highest rate of deaths per year are annually recorded from Southeast Asia, India, Brazil and certain parts of Africa.[3,4] Annual death rate attributed to snake bite envenomation accounts for 1.9 per 100,000 population in Pakistan, with southern part of the country affected the most.[5]

Since ages, snakes have remained closely linked to humans in the form of panic and fear, an icon of worship, a source of earning and a treatment. The reliance on nature for finding cure to is as old as history of mankind. Traditional remedies to cure snake bite envenomation include local skin incisions, applying leaves or sap of medicinal plants, chewing bark or drinking extracts of plants. Since the incidence of snake bite is high in sparsely populated suburbs and rural habitats, owing to prevalent illiteracy,

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inadequate and costly specialized healthcare system, wide cultural perceptions and subjective health beliefs, many inflicted people resort to traditional remedies. Unfortunately, many a time, not only are they ineffective, but also contribute to a significant delay in management and compound morbidity.

The objective of our study was to create awareness of this common, treatable, potentially fatal public health hazard and elaborating the associated patterns of morbidity and mortality in our settings. It will help to draw clear guidelines to prepare and plan for seasonal snake bite contingency in terms of availability of antivenom and other supplies in the endemic regions.

Patients & Methods

A record of all snake bite inflicted patients reporting from various parts of the district Muzaffarabad was maintained. A detailed history of time of infliction of bite, type of snake (if witnessed), any first-aid or traditional remedy attempted, mode and duration of referral, clinical and laboratory parameters upon arrival in the hospital, dose of antivenin injection, its related hypersensitivity, the need for mechanical ventilation and the outcome of treatment were documented. Laboratory parameters included complete blood counts, urine routine analysis, serum prothrombin time and APTT, serum urea and creatinine. We applied Cockcroft Gault equation to calculate creatinine clearance from serum creatinine of each patient. Serial electrocardiogram of each patient was performed to record for evidence of cardio toxicity.

IBM SPSS version-22 was used to maintain and analyze the data. Descriptive statistics were applied to find out the frequencies of age, gender, clinical and laboratory parameters. Cross tabulation was applied to find gender-wise levels of creatinine clearance. Independent sample t-test was applied to compare the mean hemoglobin between the two genders. Pearson bivariate analysis was applied to establish statistical correlation between various parameters with respect to hemorrhage. Bivariate analysis was also used to establish a correlation between traditional remedy (if any provided) and the delay (in hours) in referral to tertiary care facility. Level of significance was kept at a p-value of 0.05

Results

All victims of snake bite were transferred from various districts of Muzaffarabad and managed at Sheikh Khalifa Bin Zayed Al Nahyan Hospital, Muzaffarabad (Azad Jammu and Kashmir) from June 2017 till December 2018. Out of 79 patients 62% (n=49) of these patients were females and 38% (n=30) were males. Mean age was 33 years (SD±11.88); the youngest patient was 12 years old and the oldest was 70.

Fang marks were seen in 84.8% (n=67) patients. Local skin incision had already been made with an intent to evacuate the venom in 7.6% (n=6) of the patients. The remaining 7.6% (n=6) victims could not show any convincing evidence of a fang mark. Majority of our patients were bitten between dusk to sunrise 60.8% patients (n=48). Out of these 77.2% patients (n=61) received bite on the lower limbs. Upper limb injury was recorded in 20.3% (n=16) victims. Other body areas were involved in 2.5% (n=2) of the total patients.

Our patients shared some commonalities from the spectrum of clinical features (Figure 1). Patients who had been brought into the hospital in a state of subnormal sensorium were 2.5% (n=2). 6.3% (n=5) had clinical evidence of ptosis, 3.8% (n=3) had power grade less than 5 in any of the limb extremities. Blood pressure lower than normal was recorded in 24.1% (n=19). Only 5.1% (n=4) were hypo-ventilating, however, tachypnoea was observed in 13.9% (n=11) patients, probably attributed to anxiety and apprehension.

Out of all patients 20.3% (n=16) had gross hematuria following snake bite. Clinical evidence of epistaxis was present in (n=11) 13.9%. Pearson bivariate analysis revealed a statistically significant correlation between gross hematuria and epistaxis in our patients (p-value 0.027).

Male patients mean hemoglobin was 12.16g/dl (SD±1.724), and the females 10.53g/dl (SD±1.688). An insignificant difference was observed between the platelet counts of the two genders (p-value 0.995); male patients had mean platelet count of 180.93 x 10^9/L (SD±78.53), and females had 181.04 x 10^9/L (SD±66.50).

Mean prothrombin time was 19.51 seconds (SD±6.25). Maximum PT was 39 seconds. Mean APTT was 39.99 seconds (SD±7.34). Maximum APTT was recorded at 64 seconds. All patients with deranged coagulation were administered fresh frozen plasma, in addition to antivenom.

Patients who displayed skin changes like swelling of affected region were 35.4% (n=28). 17.7% (n=14) developed vesicles and sloughing over the affected area of the skin. Patients who demonstrated no skin change were 45.6 %(n=36).

Mean serum urea was found to be 10.30mg/dL (SD±5.16). Minimum levels being 4mg/dl and

maximum were 24mg/dL. Serum urea was significantly subnormal in 19% of patients (n=15). Normal serum urea levels were seen in 74.7% (n=59). However, a high serum urea was observed in 6.3% (n=5).

Mean serum creatinine level was 136.26µmol/L (SD±71.83). Maximum levels being 402µmol/L. 32.9% (n=26) had a normal serum creatinine. The levels were higher than normal limits in 65.8% of patients (n=52).

Creatinine clearance was found to be subnormal in 83.33% (n=25) males and 93.75% (n=45) females (Table-1).

Table-1: Patient's gender * Creatinine Clearance range Cross tabulation

Patient's gender	Creatinine Clearance Range			Total
	Less than 88 ml/min	89-97 ml/min	More than 98 ml/min	
Male	23	2	5	30
Female	45	1	2	48
Total	**68**	**3**	**7**	**78**

T-wave inversion with significant brady-arrhythmia was noted in 10.1% (n=8) patients.

From the clinical presentations it was evident that majority of our cases exhibited features of coagulopathy, cytotoxicity, renal complications and local skin changes. We encountered fewer patients with neurological symptoms. This phenomenon indicates a possible predominance of snakes from family Viperidae and Colubridae as compared to of Elapidae in this region

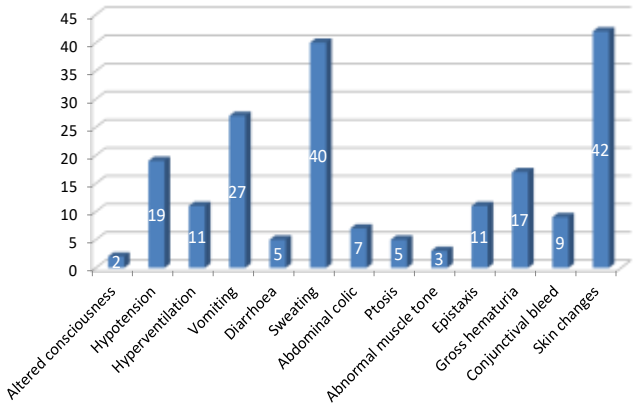

Figure 1. Clinical features in Snake Bite Patients

Urbanization has contributed to decline in prevalence of snake bite. Most of the victims belonged to rural suburbs with abundant cultivated land, shady marshes and creeks 13.9% (n=11) were brought from Garrhi Dopatta, 11.4% (n=9) were brought from Pattikka, 8.9% (n=7) were transferred from Chattar. 5.1% (n=4) patients reported from Chikaar and Chinaari respectively. Only 2.5% (n=2) patients reported from Muzaffarabad city during this period. Mean duration since infliction of snake bite till arrival in hospital was 9.975 hours (SD±6.10), and the maximum duration was 28 hours. Out of 79 patients of study group, 75.9% patients (n=60) had already sought traditional (alternative) management. Time from infliction of snake bite till arrival at hospital did not correlate significantly to traditional treatment (p-value 0.931). Fifty seven percent had received first-aid medical treatment at primary care facility that included fastening a tourniquet around the affected limb. Majority {40.5% (n=32)} had tourniquet tied up for not more than 6 hours. Mean dose of antivenom administered to the patients was 8 vails (SD±4); maximum dose delivered to individual patient was 12 vails. Only 21.5% (n=17) patients did not receive antivenin. Hypersensitivity to antivenin was experienced by 6.3% (n=5). Due to respiratory paralysis, 2.5% (n=2) patients were placed on mechanical ventilation. These patients did not recover despite aggressive intervention.

Discussion

Inconsistent epidemiologic data is available on snake bite in Pakistan. However, most prevalent snake bite regions of the country are the provinces of Sindh and Punjab.[6,7] True global incidence of snake bite and envenomation and associated morbidity is perhaps impossible to estimate due to poor methodology for estimation, insufficient hospital database and returns, and scarce resources in various snake infested regions of the world.[8]

Snakes belong to the suborder *Serpentes* of the order *Squamata* of class *Reptilia*. 67 known species of snakes inhabit in Pakistan. Notable terrestrial and sea snakes in Pakistan are boas (family *Boidae*), colubrids (family *Colubridae*), kraits and cobras (family *Elapidae*), sea snakes (family *Hydrophiidae*), thread snakes (family *Leptotyphlopidae*), pythons (family *Pythonidae*), blind snakes (family *Typhlopidae*) and vipers and pit vipers (family *Viperidae*).

Snake bites are common and carry a significant morbidity and mortality. Usually a snake bites in self-

defense if provoked or when surprised. A spectrum of 25 different enzymes is known to constitute the snake venom. However, no single snake venom contains all of them.[9] Physiologically snakes' venom may be grouped as cytotoxic, hemotoxic, neurotoxic and proteolytic.

Cytotoxic venom contains phospholipase enzymes that cause rupture of cell membrane; cardiotoxins bind at specific sites of myocardium to cause persistent depolarization, preventing myocardial contraction, and hemotoxic venom may cause red cell destruction and induce disseminated coagulation.[10] Envenoming from vipers results in hemolysis, tissue necrosis and sepsis. One third of the victims' experience vomiting and facial swelling lasting from 42 to 72 hours. Pain and blistering over the affected limb can last for 2 to 4 weeks. Bleeding from gums or epistaxis is common. Patient usually dies of septicemia or cardio-respiratory complications over 1 to 14 days of bite.

Vipers are primarily nocturnal but may remain active till dusk.[10] Cobra venom is post-synaptic neurotoxic, thereby blocking acetyl cholinesterase. As the depolarizing impulse arrives at the nerve terminal it causes release of acetylcholine from the pre-synaptic vesicles. At the synaptic cleft this acetylcholine binds to receptors and carries the impulse across the synaptic cleft. In the post-synaptic dendrite, the acetylcholine is destroyed by the enzyme acetyl cholinesterase (AChE). Fasciculins are neurotoxins that wipe out acetyl cholinesterase (AChE), consequently acetylcholine accumulates at the axonal synapse leading to fasciculation and potentially lethal spasm. Dendrotoxins found in mambas block positive and negative ions across the neuronal membrane causing nerve paralysis. α-neurotoxins found in cobra venom attack nicotinic receptors blocking acetylcholine thereby causing numbness and paralysis.[11]Symptoms progress from headache, nausea, blurred vision, vomiting, headache, abdominal pain, weakness, collapse and convulsions. The venom can cause respiratory paralysis and death as quickly as in thirty minutes.

Cobras are diurnal, mostly active at dawn and dusk. Krait venom contains neurotoxin 16 times more potent than that of a cobra. Kraits are essentially nocturnal, and their venom is pre-synaptic neurotoxic.[12] Pythons and boas restrain the prey by wrapping around coils of its body and asphyxiating the victim to death. Colubrid venom is hemotoxic, and exsanguination is the leading cause of death from colubrid bite.

Snake bite may not necessarily cause envenoming. It is assumed that envenoming comprises only one third of snake bites. 18 to 30% of snake bites in Pakistan are venomous while more than 1000 deaths per year have been attributed to envenoming.[8] This number may not be a true indicator of the exact figure due to poor reporting from various parts of the country.

Traditional healers are sought for the for the initial treatment of snake bite in many parts of the world.[13,14] In the underdeveloped world, up to 68% to 80% of inhabitants inflicted with snake bite seek traditional remedies to neutralize the effect of snake venom.[15,16]Applying barks, crushed vines and extracts of plants (*Bauhinia Cumanensis, Barlerialupulina* and *Aristolchia Rugosa*) and their tinctures, roots of *Cecropia Peltata*, chewing tobacco leaves (*Nicotiana tabacum*), have been in practice for centuries. Making incisions around the fang marks for sucking the venom out has also been performed but is strictly discouraged.[17] Since antivenin is the only specific remedy against snake venom, many times traditional procedures result in critical delay in the specific management. Many snake bite victims succumb due to useless and sometimes dangerous first aid measures in rural setups. Our study however did not establish a significant correlation between traditional management and the delay in referral, due to the fact that a considerably large number of the victims had invariably received this type of remedial intervention irrespective of the time span involving referral.

Azad Jammu and Kashmir are one of the most productive cultivation regions of the country. People earn their living by rearing cattle, herding, tilling and farming. In rural Azad Jammu and Kashmir, women share the major responsibility of agricultural activity by working in the fields. Like in many sub-tropical countries, a surge in incidence of snake bite has been noticed in harvesting season. (18) 62% of the victims in our study were female and 83.6% of them were younger than 40 years of age. More often the victims sustain bite on their lower limbs. Our results are comparable to other studies.[19] Identifying the snake has considerable importance in management, but most of the times it is virtually impossible. Snake bites have usually been reported after sunset.[20] Since most victims of envenoming are young, the morbidity also puts a considerable economic burden on the family.[8] Simpson drew attention on another very important feature by highlighting insufficient knowledge and technical expertise possessed by medical care providers about the administration of antivenin to snake bite victims in the Indo-Pak subcontinent.[21]Fastening a tourniquet around the

bitten limb with an aim to provide first aid can be disastrous in case of a cytotoxic snake venom.[22]

Conclusion

Azad Jammu and Kashmir has high incidence of hemotoxic and cytotoxic snake bite related complications. Morbidity is attributed to lack of community awareness about prevention, high treatment costs and travelling expenses, inaccessibility to hospitals from far flung areas, cultural beliefs about traditional remedies and ill-equipped primary and secondary care centers in the rural areas. There is a need to improve accessibility, disseminate knowledge, and clinical and technical skills to address a very widespread yet lethal public health hazard.

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- Munazza Nazir — Conception, Study Designing, Planning, Experimentation, Study Conduction, Analysis, Interpretation, Discussion
- Nadeem Ahmed Sheikh — Conception, Study Designing, Planning, Experimentation, Study Conduction, Analysis, Interpretation/ Discussion
- Rubina Rafique — Analysis, Interpretation, Discussion
- Muhammad Ilyas — Conception/ Study Designing/ Planning, Experimentation/ Study Conduction, Analysis, Interpretation, Discussion
- Bashir Ahmed Trumbo — Analysis, Interpretation, Discussion
- Kanwal Nadeem — Analysis, Interpretation, Discussion