Research Paper: Snake Envenomation in North-West Iran: A Three-Year Clinical Study

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ABSTRACT

Background: Snakebite is a medical emergency and must receive high-priority assessment and treatment, even in patients who initially appear well. A few reports have been published regarding snakebite in Iran. This study aimed to assess the snakebite cases in a tertiary teaching hospital in the northwest of Iran.

Methods: We assessed demographic and clinical characteristics of adult patients who were admitted because of snakebite into Ayatollah Taleghani Teaching Hospital, Urmia, West Azerbaijan, Iran, between January 1, 2012, and December 31, 2014. After institutional Ethics Committee approval, the required data were extracted, analyzed, and reported.

Results: Totally, 60 snakebite cases were recorded during three years study period, of them 63.3% were male. The patients' Mean±SD age was 37.8±15.8 years. The majority of snake envenomations occurred in the farms and mountains (71.4%), frequently in the afternoons of spring and summer seasons, and mostly affected inhabitants or visitors of the rural areas. The Mean±SD time interval between snake envenomation and admission to the first health center was 15.3±28.6 hours. The anatomic sites of the snakebite were lower and upper extremities in most instances (96.6%). Only 5 (8.3%) patients had severe toxicity, and 2 patients underwent surgical fasciotomy. The patients were treated using antihistamines (n=45), corticosteroids (n=35), antibiotics (n=54), polyvalent snake antivenins (n=50), wound care and tetanus immunization (n=39). The Mean±SD number of polyvalent snake antivenins used for each patient was 3.3±1.9 (range, 1-8) vials. There was no in-hospital fatality.

Conclusion: Most snakebites victims in the northwest of Iran were men in their productive age. Early diagnosis and proper use of snake antivenins could be life-saving and should be encouraged.

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1. Introduction

Snakes belong to a widespread group of reptiles that are found in almost every part of the world, except small areas such as Antarctica or some isolated islands [1-3]. There are around 3500 species of snakes around the world from which less than 10% are poisonous [1, 4, 5]. Venomous snakes have a pair of teeth (fangs) that works like an enlarged needle to inject their venom deeply, especially subcutaneously or intramuscularly into the tissues of the victims and humans [1, 6, 7]. The injection of the toxin causes a variety of symptoms from mild toxicity to critical systemic response depending on the type of snake, venom volume, season, victim's age and physical status. Clinical presentations of the snakebites may differ from almost none, dry bite, to severe systemic complications such as shock, infection, coagulopathies, neuropathies, cardiomyopathy, renal failure, rhabdomyolysis, and even death [6, 8-10].

Snakebite is a significant health emergency, especially in rural areas of developing countries. Hence, the World Health Organization (WHO) mentioned snakebite management as one of its priorities [6, 11, 12]. It is estimated that every year around 2.1 to 5.5 million people were bitten by snakes in the world from which 20000 to 125000 die and thousands of them develop chronic disabilities, including 400000 amputations [2, 13, 14]. Only in Asia, the reported annual number of snake envenomations and resulting deaths are approximately 2 million and 100000 cases, respectively [2].

Iran is also a country with high reported cases of animal bites as well as snake envenomation. It is estimated that Iran has a variety of 69 species of snakes with 9 semi-venomous and 25 venomous (including The Persian Gulf water snakes) species [1, 15]. The number of snakebites in 8 years from 2002 to 2009 was reported to be around 5 to 7 thousand cases, with 3 to 9 deaths per year [4, 5]. Another study reported the number of snakebites in a decade from 2002 to 2011 to be more than 50000 cases with an incidence rate of 4.5 to 9 cases per 100000 population and 67 fatalities in a whole decade [16]. Isolated epidemiologic studies concerning snakebite are available from only some parts of the country such as Ardabil [17], Kashan [5], Queshm [18], and Tabriz [19]. This study aimed to assess snakebite cases in a tertiary teaching hospital in the northwest of Iran.

2. Materials and Methods

In this observational clinical study, we gathered registered data of all adult patients (≥14 years) with a history of a snakebite who were referred to Ayatollah Taleghani Teaching Hospital in Urmia, West Azerbaijan Province, Iran, from January 1, 2012, to December 31, 2014.

The shape of Iran on the world map resembles a cat, and West Azerbaijan Province is located at the right side of its face (Figure 1 A). The province is one of the 31 provinces of the country bordering Turkey, Iraq, and the Nakhchivan Autonomous Republic, as well as the provinces of East Azerbaijan, Zanjan, and Kurdistan. Urmia is the capital city and largest county of the province. There are also 16 other counties in the province (Figure 1 B). According to the last national census (2016), the population of West Azerbaijan Province and Urmia County was 3,265,219 and 1,040,565 people, respectively [20, 21]. Ayatollah Taleghani Teaching Hospital is the second largest public hospital in Urmia which has Clinical Toxicology, Infectious Diseases, Dermatology, Cardiology, and Internal Medicine Wards. The first three wards are the only academic referral wards in the province.

The snake envenomation was confirmed by either a clinical toxicologist or an infectious disease specialist. The required demographic and clinical data such as gender, age, address, marital status, occupation, date of admission, time of discharge, the anatomic site of snakebite, presence of fang mark(s), clinical symptoms and signs, the prescribed treatments (antihistamines, corticosteroids, antibiotics, antivenins, wound care, and tetanus immunization), surgical interventions (including fasciotomy), and complications of snake envenomation (including patient's death) were extracted from the hospital documents.

The conduction of this study was according to the Helsinki Declaration and approved by the Ethics Committee of Deputy of Research and Technology, Urmia University of Medical Sciences, Urmia, Iran. All the gathered data were analyzed in SPSS for Windows version 16 software (SPSS Inc., Chicago, IL, USA). We expressed quantitative data as Mean±SD and qualitative data as frequency and percentage.

3. Results

Overall, 60 cases of snakebite were included in the study that happened during the three years. Out of them, 63.3% were male, and 36.7% were female. The Mean±SD age of the patients was 37.8±15.8 (range: 15

Figure 1. West Azerbaijan Province [37]

A. Location of the province on the country map (Coordinates: 37.5528°N 45.0759°E); B. Counties of the province

to 72 y) years. This was 34.3±14.8 years (range: 15 to 61 y) for men (n=38) and 43.7±16.1 (range: 22 to 72 y) years for women (n=22). Assessment of marital status showed that 76.7% of the patients (25 males and 21 females) were married, and 18.3% (1 male and 10 females) were single. For 5% of the patients (3 males), the marriage status was unknown.

Regarding occupation and career, the status of 24 (40%) cases was unknown, and among remaining 36 patients, 11 (18.3%) were self-employed, 13 (21.7%) house wife, 5 (8.3%) farmer, 5 (8.3%) student, and 2 (3.3%) worker. Eleven (18.3%) patients mostly men (n=9) and 49 (81.7%) patients also mostly men (n=29) were inhabitants of urban and rural areas, respectively.

The highest number of snakebites occurred in 2013 (n=25), followed by 2012 (n=22) and 2014 (n=13). Envenomations only happened from April to October (first seven months of the solar calendar); mostly in summer and spring seasons (Figure 2). The majority of snakebites occurred during day times (afternoon: 19, noon: 12, and morning: 12 cases) and the lowest was at night with 2 cases; however, the time of 15 snakebite cases was unknown.

Most of the patients (n=42, 70%) were from Urmia County followed by other cities of the province, including Oshnavieh (n=6, 10%), Piranshahr (n=3, 5%), Sardasht (n=3, 5%), Salmas (n=2, 3.3%) as well as Khoy, Maku, Bukan, and Shahin-Dezh each with one case of snakebite (1.7%).

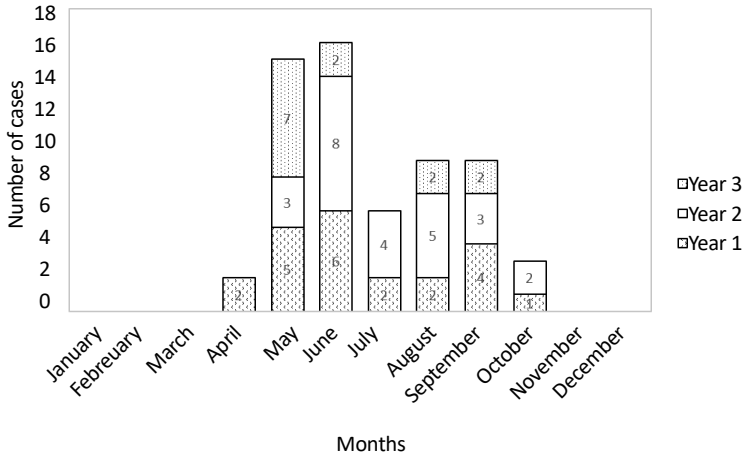

Figure 2. Frequency of snakebite by months, seasons, and year (n=60)

Table 1. Grading of clinical presentations of snakebite*

Extent of Envenomation	Clinical Observations
None (dry bite)	Fang marks may be seen, but no local or systemic symptoms after 8-12 hours
Minimal	Minor, non-progressing, local swelling, and discomfort without systemic symptoms or hematologic abnormalities
Moderate	Progression of swelling beyond the area of bite with local tissue destruction, hematologic abnormalities, or non-life-threatening systemic symptoms
Severe	Marked progressive swelling, pain with or without local tissue destruction Systemic symptoms such as nausea, vomiting, diarrhea, malaise, weakness, dysrhythmias, hypotension, convulsions, severe coagulopathy

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* Classification presented here is adapted and summarized from references number [1, 6, 12, 22, 23, 34, 35].

In case of referral to the Ayatollah Taleghani Hospital, 48 patients (80%) were referred by themselves, 7 (6.7%) by other hospitals in Urmia city, 4 (6.7%) from other counties in the province, and 1 (1.7%) was transferred by emergency medical service to the hospital. The Mean±SD time interval between the snake envenomation and admitting to the first health center was 15.3±28.6 hours (n=49, range: 30 min to 5 days). One patient re-admitted due to the complication of the snakebite after 16 days and two other cases after one month which were not included in this calculation. For 8 patients the data were not available.

The place of snakebite occurrence was only recorded in 42 cases from which, 21 (50%) were bitten in mountains and plains, 9 (21.4%) in farms, 5 (11.9%) in the workplaces, and 7 (16.7%) in the houses. The involved anatomic sites included lower extremities (n=33, 55%) followed by upper extremities (n=25, 41.6%), gluteal region (n=1, 1.7%), and unknown (n=1, 1.7%). The shape of fang marks have only been recorded in 22 cases; among them, 14 had one, and 8 had two punctures. According to clinical observations, the severity of snake envenomation was classified as none, minimal, moderate or severe as presented in Table 1 [1, 6, 12, 22, 23].

Majority of our studied cases had minimal toxicity (n=32, 53.3%) followed by moderate (n=12, 20%), none (n=11, 18.3%), and severe toxicity (n=5, 8.3%). Among them with severe envenomation, 3 (5%) patients had decreased levels of consciousness and disorientation, 3 (5%) developed coagulopathies, 2 (3.3%) proceeded to compartment syndrome and underwent surgical fasciotomy, 1 (1.7%) developed hypotensive shock, and 1 (1.7%) had complicated by acute kidney failure.

The following management were used for the treatment of snakebite in our studied patients: antihistamines (n=45, 75%), corticosteroids (n=35, 58.3%); antibiotics (n=54, 90%), snake antivenins (n=50, 83.3%); wound care and tetanus immunization using vaccine and or toxoid (n=39, 65%). Sensitivity reaction to antivenin administration occurred only in one case. The Mean±SD number of polyvalent snake antivenin (10 mL vials manufactured by Razi Serum and Vaccine Research Institute, Karaj, Iran) for the treatment of study patients was 3.3 (1.9) (range: 1-8) vials.

In this series, most patients were managed in the hospital wards except two cases who needed Intensive Care Unit (ICU) admission. The Mean±SD hospitalization period was 3.4±0.32 days ranging from 12 hours to 12 days. Finally, 39 (65%) patients were discharged from the hospital with complete recovery; 18 (30%) with partial improvement; and 3 (5%) upon self-consent. There was no in-hospital fatality among our studied patients.

4. Discussion

Snakebite is a major neglected public health problem in many parts of the world as well as Iran [6, 26]. However, comprehensive data in this regard need various epidemiologic assessment in different parts of the country. Our study aimed to assess some of the basic demographic and clinical features of snakebites victims in West Azerbaijan Province of Iran.

In the whole period of our research from 2012 to 2014, we studied 60 snakebite cases. This statistic is much more than a similar survey in Kashan with 50 patients for 8 years [5]. Another study in Ardabil from 2008 to 2013 reported 67 snakebite cases in 6 years [17]. A survey in Qeshm, a southern island in Iran, reported 110 cases of

snakebite from 2011 to 2017 [18]. Another study from the leading referral toxicology center of the country (Loghman-Hakim Drug and Poison Information Center, Tehran, Iran) reported only 70 cases of snakebite during 4 years from March 2007 to March 2011 [27].

Furthermore, Alavi et al. (2008) reported the total number of snakebites during 1997-2006 in Khuzestan to be 39 cases; however, it seems that they missed several documents due to the retrospective manner of their study and incompetency of the presented data [28]. Statistics that have been reported from Haji-Abad, a city in Hormozgan Province, showed that the total number of snakebites between June 2012 and August 2016 was 195 cases [29]. Another study was conducted in Tabriz, East Azerbaijan Province, Iran from 2002 to 2012. They reported the total number of snakebites to be 160 cases in 10 years [19].

According to a country based assessment, the frequency of snakebites in Iran was 4.5 to 9.1 per 100000 population during 2002-2011. This study reported 53737 snakebite cases during these 10 years. The highest incidence of snakebite occurred in Khuzestan Province with 926 cases from 2011 to 2012 followed by Sistan and Baluchestan Province with 502 cases, and Hormozgan Province with 466 incidents. West Azerbaijan had stood at the 14th place with 117 cases after Golestan Province with 122 cases [16]. However, no similar comprehensive study was reported from Iran in recent years.

Most of our studied patients were male (63.3%) which is consistent with other reports from Khuzestan [28] with 62%, Hormozgan [29] with 70%, Ardabil [17] with 76%, Tabriz [19] with 77.6%, and Tehran [27] with 82.8% male predominance. The highest reported ratio belonged to Qeshm study where 92% of patients were male [18]. Also, the total statistic of Iran shows that about 70% of snakebites victims are men [16].

Snakebite is also a significant and common problem in South and South-East Asia like Nepal, Singapore, and India [2, 30]. Studies in Singapore [31] and Nepal [32] report the percentages of the males to be 83% and 53%, respectively, which are in line with the findings of this study. Contrary to the results of our study, a study in India reported that the majority (60%) of the victims were females [33]. To the best of our knowledge, most kinds of intoxications are more common in women than men in India which makes India an exception in this regard.

We found 37.8±15.8 years as the Mean±SD age of the patients in this study. Similarly, Khuzestan study reported the median ages of the patients were 24.4 years for men and 26.2 years for women [28]. In Loghman Hakim Hospital in Tehran, all patients were older than 20 years [27] but they did not study pediatric age group like us. Farzaneh et al. (2017) reported the Mean±SD age of the patients with snakebite in Ardabil as 35.6±16.5 years [17]. The total statistic of Iran shows that most snake envenomations occur in 15-24 years followed by 25-34 years age groups [16].

The high prevalence of snake bites (71.4%) in of the rural areas was consistent with the study of Ebrahimi et al. (2018) who reported 80% occurrence in rural places and national statistics in which 70% of snake envenomations had occurred in rural places of Iran [16, 29].

Our results showed no trending pattern regarding the frequency of the snakebite in different years of our study; the peak of the frequency was in 2013 with 25 cases. Furthermore, the highest number of snake envenomation was in June with 16 cases followed by May with 15 cases. However, the study in Qeshm reported the highest number of bite frequency in June, July, August, and September [18]. The moderate mountainous climate of our region causes most of the snakebites to take place in spring and summer.

Most of the hospital admissions in our study occurred in the afternoon, and the least at night. However, in Qeshm study, most of the referrals to the hospital occurred at night [18]. Ebrahimi et al. (2018) reported most of the cases referred to medical centers in the morning [29]. The differences in the time of admission may be related to the geographic position of the study. Qeshm is an island in which patients could reach the hospital shortly after snakebite, but our study was performed in a referral hospital in the center of a relatively large province, which is larger than many small countries alone, and distances among some cities of the province from its center is more than 350 km or 4 to 5 hours by car. The bite site was mainly on lower and upper extremities in our study. Similarly, other studies reported legs and hands as the main parts of venom injection [18, 19, 29, 34]. These areas are usually more exposed to the snakes.

Our study also investigated the clinical presentations and complications of snake envenomation. The severity of the envenomation grouped into four categories; none (dry bite), minimal, moderate, and severe (Table 1). The patients with mild presentations have edema and local tenderness; in moderate cases, they also have systemic signs such as nausea, vomiting, mild hypotension, chills, and the clue of coagulopathies without bleeding signs. In

severe cases, the patients may develop shock, bradycardia, tachypnea and distress, prominent coagulopathies with apparent bleeding [5, 34, 35].

In our study, 53% of the patients presented mild signs, 20% moderate, 18% none, and 8% severe signs. We had one case with the immediate loss of consciousness, 3 cases with coagulopathies, 2 cases with compartment syndrome leading to surgical fasciotomy, 1 case with hypotensive shock, and 1 case with acute kidney failure. Zamani et al. (2016) listed the frequency of systemic signs from the most occurred to the least occurred as vomiting, tachycardia, hematuria, fever, paresthesia, hypotension, and diarrhea [27].

Ebrahimi et al. (2018) categorized systemic signs as sympathetic, parasympathetic, and Central Nervous System (CNS) signs. Five percent of the patients showed CNS signs, 4% demonstrated sympathetic signs, and 2% parasympathetic signs [29]. However, the latter study was conducted in south Iran, where snake fauna may be different from our region. It is noteworthy that, no poisonous snake from the Elapidae family such as the Caspian Cobra (Naja oxiana) is found in northwest Iran and all venomous snakes of the region belonged to the Viperidae family. Furthermore, among the 14 known vipers in Iran, three are named according to the name of cities of the province; the viper of Urmia, the viper of Takabi, and the viper of Khoy.

Most of the studies missed the details of treatment. Our study has some data in this regard. Antibiotics were prescribed in 90% of the patients; however, some studies report that prophylactic antibiotic is not indicated for snakebite [1, 36, 25]. Furthermore, prophylactic corticosteroid prescription is not advised except for people with sensitivity reactions [22, 36, 25]. Although antivenin injection was accomplished for 83.3% of the patients, only 2% of the patients showed a sensitivity reaction in our study. Studies also report that these reactions only occur in 3% of the injected cases [1]. Zamani et al. (2016) administered antivenom for 97.1% of their patients in Loghman Hakim Hospital, Tehran [27]. It seems that some of our patients, especially those with no or minimal extent of snake envenomation, might be treatable without using antivenin.

While there was no in-hospital fatality in the current study, Zamani et al. (2016) reported 1.4% mortality rate in Loghman Hakim Hospital, Tehran [27]. Dehghani et al. (2014) reported 67 death among 53787 snakebite during 2002-2011 which is equal to 0.12% mortality rate for the country [16].

The current study can further complete the existing data on the epidemiology of snakebite in Iran; however, its retrospective manner was one of its limitations. Some of the crucial data were incomplete due to this restriction. Also, our study cannot demonstrate the real number of snake bites in Urmia because some of the patients may be referred to other treatment centers and this study was limited to the cases older than 14 years. Fortunately, the attention of authorities in the Ministry of Health and Medical Education of Iran has recently been focused on the issue of poisonous animal bites, including snakebite. Therefore, another study, especially perspective one with a longer duration may present better results. Nonetheless, a better registry system is necessary to overcome the limitations in this field.

5. Conclusion

Snakebite is a significant public health problem in Urmia and West Azerbaijan. It is an outdoor problem mainly affect men of reproductive age. It may accompany local or systemic signs that can be graded. We suggest that people, especially in rural areas, be trained and educated about venomous snakes, prevention of bite, and the importance of early hospital referral and treatment of victims.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Deputy of Research and Technology, Urmia University of Medical Sciences, Urmia, Iran. We also followed the principles outlined in the 1964 Helsinki Declaration and its later amendments.

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Authors contributions

Literature review, data acquisition, analysis: Anita Aminizadeh; Preparing English draft of the manuscript: Mehrdad Sahranavard; Critically revised the draft for important intellectual content: Rahim Nejad-Rahim, Mohammad Delirrad; Finalizing the manuscript for English style and language: Mohammad Delirrad; and Reviewing and approving the final draft and submitted version of the manuscript: All authors.

Conflict of interest

The authors declared no conflict of interest.

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