ORIGINAL ARTICLE

# Severity and Management of patients with Snake and Scorpion Envenomation Admitted to an Intensive Care Unit in Southeastern Turkey: A retrospective study

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## Abstract

*Background:* Snake and scorpion envenomation is a common public health problem in many regions of the world. Life-threatening emergencies may occur in patients with snake and scorpion envenomation; therefore, these patients may be required intensive care unit (ICU) follow-up. Our objective was to present the demographic and clinical characteristics, treatment modalities and short term outcomes of patients with snake and scorpion envenomation who followed up in our tertiary hospital ICU.
*Methods:* Patient records were retrospectively searched and snake or scorpion envenomation patients with ICU stay were identified with relevant keywords and ICD-10 codes between January 2010 and September 2019. All cases with ICU stay were included for study analysis, regardless of patient age. Scorpion and snake envenomation managed in outpatient clinic were excluded from our data. Poisoning severity score (PSS) system was used to present signs and symptoms and PSS was calculated. Primary and critical care treatment modalities were identified and analyzed.
*Results:* Forty patients (25 with snake bites [62.5%] and 15 with scorpion sting [37.5%]) were included in this retrospective study. Local and systemic effects have been reported in 33 (82.5%) and in 27 patients (67.5%), respectively. Majority of patients suffered from pain or disturbances in sensory neural, hematological, cardiovascular or metabolic systems. Median PSS was 2 (0-4) and median length of stay in ICU was 2 days (1-12). Mortality rate was 2.5%. Antivenom immunoglobulins (n=32, %80.0), systemic antibacterial agents (n=24, 60%), and paracetamol (n=21, 52.5%) were the most common systemically administered treatments. Surgical interventions were performed in 4 patients (10%)
*Conclusions:* We reported that snake and scorpion envenomation were mostly admitted to the ICU with local and/or systemic symptoms for advanced monitoring and observation. Although life treating emergencies and mortality was uncommon in our study, we think that these patients should be closely followed up in ICU.

**Keywords:** Venom, poisoning, critical care, Middle East, scorpions, snakes, envenomation

**How to cite this article:** Bozkurt FT, Aydin B, Tanriverdi TB, Patmano G, Tercan M, Kaya A. Severity and Management of patients with Snake and Scorpion Envenomation Admitted to an Intensive Care Unit in Southeastern Turkey: A retrospective study. ***Asia Pac J Med Toxicol*** **2021; 10(2):38-43.**

## INTRODUCTION

Envenomations due to scorpion sting and snake bite constitute around two percent of poisoning cases.[1-3] Medically important scorpion and snake species vary regionally and envenomation patterns are dependent on the season, responsible species, and patient characteristics.[4,5] In Turkey, Androctonus crassicauda, Leiurus quinquestriatus, Mesobuthus gibbous, and Mesobuthus eupeus are the scorpion species of medical importance related to envenomations[6] whereas Viperidea family is mostly responsible for snake envenomations.[4] Southeastern Turkey is of special interest for snake and scorpion envenomations due to the specific fauna, arid climate and rural socioeconomical factors of the region. These features are also typical for the area of Middle East.[7-9]

Management of snake and scorpion envenomations in Turkey is guided mainly by the poisoning management guidelines for primary care centers and consultation with National Poison Information Center.[2,10] While this guidance provides primary treatment algorithms in detail, Guidelines/ instructions for referral and management of patients with severe systemic symptoms and signs along with admission criteria to intensive care unit (ICU) are largely lacking.

Our objective was to present the demographic and clinical characteristics, treatment modalities and short term outcomes of patients with snake and scorpion envenomation who followed up in our tertiary hospital ICU.

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## METHODS

The design and protocol of this observational retrospective cohort study was approved by Harran University Ethics Committee (04/11/2019-04/21). Patients' medical records of Sanliurfa Mehmet Akif Inan Hospital were screened for scorpion and snake envenomations between January 2010 and September 2019 with relevant keywords ( scorpion, snake, poisoning) and ICD-10 codes(X22,T63.0, T63.2). Regardless of patient age, all cases with ICU stay were included for study analysis. Scorpion and snake envenomation managed in outpatient clinic were excluded from our data. ICU admissions were decided by the responsible intensivists in accord with NPIC (National Poison Information Center) recommendations. Variables for demographics, envenomation history, presenting symptoms and signs, treatments, and outcomes were recorded. European Association of Poison Centers and Clinical Toxicologists/ International Programme on Chemical Safety Poisoning Severity Score (PSS) system definitions were used for classification of local and systemic effects and PSS was calculated for each case with the most severe symptomatology, as recommended.[11] Electrolyte and fluid disturbances (Hyponatremia or hypernatremia) were defined as serum sodium level <135 mg/dl and hypernatremia >145 mg/dl.[12] Demographical and clinical characteristics were presented as percentage and number or median (25-75.$^{th}$ interquartile range). We did not perform statistical comparisons between snake and scorpion envenomation patient groups as we aimed to provide descriptive exploratory information. Data analysis was performed with IBM SPSS Statistics (version 20; IBM Corporation, Armonk, NY) software.

## RESULTS

A total of forty patients were identified with a history of snake (n=25, 62.5%) or scorpion (n=15, 37.5%) envenomation and ICU stay. Median age was 30 (range: 9-68) and all patients were adults except for one. Forty-five percent of the patients were female. Two patients (5%) were pregnant (one in the second and one in the third trimester). Majority of the envenomations occurred in rural areas (n=30, 75.0%) and in summer (n=24, 60%). Lower extremities were the bite or sting area in 23 patients (57.5%), upper extremities were the bite or sting area in 13 patients (32.5), and head and neck were the bite or sting area in 1 patient (%2.5). Median duration of time to from envenomation to attendance to the health center was 1.0 hour (0.5-24.0). All cases were consulted with the National Poison Information Center yet the specific recommendations were missing. All patients' demographic and clinical characteristics ,**anatomical site of sting or bite, envenomation in a rural area, length of stay in intensive care** are presented in Table 1.

**Table 1. Patient demographics and envenomation characteristics**

| Characteristics | All patients (n=40) | Scorpion envenomation (n=15) | Snake envenomation (n=25) |
|---|---|---|---|
| Age, median (range) | 30 (9-68) | 22 (15-52) | 33 (9-68) |
| Gender (females), n (%) | 18 (45) | 8 (53.3) | 10 (40.0) |
| Envenomation in a rural area, n (%) | 30 (75) | 10 (66.7) | 20 (80) |
| Calender season of envenomation, n (%) | | | |
| Winter | 1 (2.5) | 1 (6.7) | 0 (0) |
| Spring | 5 (12.5) | 1 (6.7) | 4 (16.0) |
| Summer | 24 (60.0) | 10 (66.7) | 14 (56.0) |
| Autumn | 10 (25.0) | 3 (20.0) | 7 (28.0) |
| Anatomical site of sting or bite, n (%) | | | |
| Head and neck | 1 (2.5) | 0 (0) | 1 (4.0) |
| Upper extremity | 13 (32.5) | 4 (26.7) | 9 (36.0) |
| Lower extremity | 23 (57.5) | 11 (73.3) | 15 (60.0) |
| Time to index healthcare service (hours), median (range) | 1.0 (0.5-24.0) | 2.0 (0.5-6.0) | 1.0 (0.5-24.0) |
| Presence of pregnancy, n (%) | 2 (5) | 2 (13.3) | 0 (0) |
| Poisoning severity score, n (%) | | | |
| 0 or 1 | 19 (47.5) | 9 (60.0) | 10 (40.0) |
| 2 | 16 (40.0) | 6 (40) | 10 (40.0) |
| 3 or 4 | 5 (12.5) | 0 (0) | 5 (20.0) |
| Presence of local effects, n (%) | 33 (82.5) | 11 (73.3) | 22 (88.0) |
| Mild or moderate pain | 24 (60.0) | 9 (60.0) | 15 (60.0) |
| Swelling | 21 (52.5) | 3 (20.0) | 18 (72.0) |
| Reddening | 9 (22.5) | 4 (26.7) | 5 (20.0) |
| Necrosis | 2 (5.0) | 0 (0) | 2 (8.0) |
| Presence of systemic effects, n (%) | 27 (67.5) | 11 (73.3) | 16 (64.0) |

**Table 1. Continued.**

| Characteristics | All patients (n=40) | Scorpion envenomation (n=15) | Snake envenomation (n=25) |
|---|---|---|---|
| Paresthesia | 8 (20.0) | 8 (53.3) | 0 (0) |
| Coagulation disturbances without bleeding | 7 (17.5) | 3 (20.0) | 4 (16.0) |
| Mild acidosis | 7 (17.5) | 1 (6.7) | 6 (24.0) |
| Sinus tachycardia | 6 (15.0) | 0 (0) | 6 (24.0) |
| Thrombocytopenia | 5 (12.5) | 1 (6.7) | 4 (16.0) |
| Mild electrolyte and fluid disturbances (Hyponatremia or hypernatremia) | 5 (12.5) | 3 (20.0) | 2 (8.0) |
| Sinus bradycardia | 4 (10.0) | 1 (6.7) | 3 (12.0) |
| Hypertension | 4 (10.0) | 1 (6.7) | 3 (12.0) |
| Myocardial ischaemia suspected by elevated serum troponin levels | 2 (5.0) | 1 (6.7) | 1 (4.0) |
| Compartment syndrome | 2 (5.0) | 0 (0) | 2 (8.0) |
| Others[a] | 5 (12.5) | 1 (6.7) | 4 (16.0) |
| Lenght of stay in intensive care (days), median (range) | 2 (1-12) | 2 (1-5) | 2 (1-12) |

[a]Visual disturbance (double vision) (n=1), coagulation disturbances with bleeding (hematemesis) and hypotension (n=1), hyperthermia (n=1), hypothermia (n=1), minimal rise in liver enzymes (n=1)

Local and systemic effects of envenomation were recorded in 33 (82.5%) and in 27 patients (67.5%), respectively, whereas twenty-one patients (52.5%) presented with both local and systemic signs and symptoms. Most common local effects were pain (n=24, 60.0%) and swelling (n=21, 52.5%) while paresthesia (n=8, 20%), coagulation disturbances (n=8, 20%), and mild acidosis (n=7, 17.5%) were the most commonly reported systemic effects. Echocardiography was performed in three patients (7.5%). Median PSS was 2 (0-4) with 52.5% of the patients scoring 2 or above. Median length of stay in the ICU was 2 days (1-12). Of the two pregnant patients, both were stung by scorpion, neither were administered with antivenom, and one developed trombocytopenia while the other did not develop any local or systemic effects. One patient (2.5%) with snake envenomation deceased during ICU stay due to multiple organ failure. Twenty-nine patients were discharged directly from ICU, three were transferred to internal medicine department and seven were discharged against medical advice (Table 1).

Thirty-five patients (87.5%) received tetanus prophylaxis. Antivenom immunoglobulins (n=32, %80.0), systemic antibacterial agents (n=24, 60%), and paracetamol (n=21, 52.5%) were the most common systemically administered treatments. Five patients (12.5%) required fresh frozen plasma (FFP) transfusion. Surgical interventions performed following snake bite which were involved blister or abscess incision with drainage in two patients (5%), fasciotomy in one patient (2.5%), and fasciotomy and finger amputation in one patient (2.5%). Inotropic agents and mechanical ventilation were used for one of the snake envenomation patients who eventually deceased. No adverse reaction to antivenom, patient-inflicted incision or infection found in patients' medical records. Treatment modalities employed for envenomations are presented in Table 2.

**Table 2. Treatment modalities employed for envenomations**

| Treatment modality, n (%) | All patients (n=40) | Scorpion envenomation (n=15) | Snake envenomation (n=25) |
|---|---|---|---|
| Tetanus prophylaxis | 35 (87.5) | 13 (86.7) | 22 (88.0) |
| Antivenom | 32 (80.0) | 11 (73.3) | 21 (84.0) |
| Systemic antibacterial agents | 24 (60.0) | 5 (33.3) | 19 (76.0) |
| Paracetamol | 21 (52.5) | 5 (33.3) | 16 (64.0) |
| Histamine antagonists | 16 (40) | 9 (60.0) | 7 (28.0) |
| Systemic corticosteroids | 13 (32.5) | 5 (33.3) | 8 (32.0) |
| Nonsteroidal anti-inflammatory drugs | 9 (22.5) | 5 (33.3) | 4 (16.0) |
| Opioid analgesics | 3 (7.5) | 0 (0) | 3 (12.0) |
| Proton-pump inhibitors | 5 (12.5) | 2 (13.3) | 3 (12.0) |

**Table 2. Continued.**

| Treatment modality, n (%) | All patients (n=40) | Scorpion envenomation (n=15) | Snake envenomation (n=25) |
|---|---|---|---|
| Plasma transfusion | 5 (12.5) | 2 (13.3) | 3 (12.0) |
| Surgical intervention | 4 (10.0) | 0 (0) | 4 (16.0) |
| Others[a] | 6 (15.0) | 0 (0) | 6 (24.0) |

aRed blood cell transfusion (n=1), metoclopramide (n=1), enoxaparin sodium (n=1), vitamin K (n=1), atropine (n=1), inotropic agents and mechanical ventilation (n=1)

## DISCUSSION

Epidemiological studies conducted by the National Poison Information Center of Turkey indicate that scorpion envenomations are twice as common as snake bites[2] whereas snake envenomations constituted almost two thirds of admissions to the ICU in our study cohort. This finding might reflect that a higher proportion of snake envenomations tend to present with severe morbidity. Patient demographics, seasonality, and anatomical site of bites and stings were similar to epidemiological studies and case series from Southeastern Turkey.[4,5,7,9]

19 patients (47.5%) were detected as an initial PSS of 0 and1, 16 (40%) patients a score of 2, and 5 (12.5) patients a score of 3-4 in our study. While PSS is formally calculated retrospectively,[11] Casey et al prospectively has validated the PSS system and has indicated that the initial PSS at the time of admission predict poorer outcome. Less than one percent of poisoned patients with an initial PSS of 0 or 1 (absence of symptoms or mild effects) developed PSS 2 (moderate effects) over the course of their follow-up with no deterioration to severe symptomatology.[13] The findings of this study however should be examined carefully as responsible poisoning agents are not presented and observed predictive power of PSS system do not apply for snake and scorpion envenomations.

Majority of envenomation patients suffered from pain or disturbances in sensory neural, hematological, cardiovascular or metabolic systems. Given the fact that only a third of the patients required respiratory or cardiovascular support, transfusion or surgical intervention, the majority of the patients with envenomation effects were admitted to the ICU mainly for advanced monitoring with a median follow-up of two days. These findings of envenomation symptomatology and management are similar to the results of previous reports of snake or scorpion envenomations followed up in an ICU in Turkey.[14,15] Predictive value of Poisoning Severity Score for further course of envenomation could be also more useful to determine ICU stay duration to better allocate critical care resources. A similar conclusion was reached for scorpion envenomations and ICU admission was recommended only for patients with systemic effects by Tutak et al in 2018 .[16] However, these conclusions could only be applied for adult patients as envenomation of children results in disproportionately more severe presentations and clinical courses, which require more intense monitoring and treatment approaches.[17-19]

Eighty percent of the patients were administered antivenom immunoglobulins as part of envenomation treatment. Similar or higher rates of antivenom use, sometimes given to all as routine prophylaxis, in adults or children were reported previously within the same geographical region of Turkey.[7,9,14-16,18-21] Due to lack of prospective controlled clinical trials of antivenoms corresponding to Middle East fauna, recommendations vary regarding the use, posology, and administration route of snake and scorpion antivenoms.[22] Poisoning management guidelines of Turkey recommend snake or scorpion antivenom only for the cases developing severe or progressive local or systemic effects.[10] Product characteristics of snake and scorpion antivenoms available in Turkey (ACSERA, POLISERA, ALVENOAC, ALVENOBAL) also recommend the antivenom use for mild to severe cases or only in the presence of systemic effects with safety cautions of potential acute reactions, delayed serum sickness, and viral exposure related to antivenom administration. However, these product information do not provide any clinical efficacy or safety data. In a prospective study conducted by Açıkalın et al., the systemic administrations of snake antivenom were only applied to moderate and severe envenomations and complete recovery of all cases were reported.[23] While antivenom use for snake or scorpion envenomation in Turkey has been generally regarded as safe with no adverse events reported in several case series,[8,9,18-20,24] allergic reactions and severe anaphylaxis to snake antivenom have been reported in prospective studies at the rates of 4.1% and 17.8% respectively .[21,23] While no specific adverse effects related to antivenom administration were mentioned in our patient medical records , we cannot exclude the possibility of histamine antagonists and corticosteroids use for aversion or treatment of antivenom-related reactions in some patients. Large nationwide randomized and controlled clinical trials and prospective observational studies are needed to determine the safety, efficacy, and optimal use of available antivenom preparations. Guideline recommendations of World Health Organization for the Clinical assessment required for antivenom application/administration and its considerations could be consulted considered for study designs and determining their endpoints.[25]

An unexpected finding of our study was the common use of systemic antibacterial agents for envenomations. Since there is no report of infection found in our patients medical records, it has been concluded/can indicate that the antibacterial

agents were mainly administered for prophylaxis. While poisoning guidelines do not recommend routine use of antibacterials for prophylaxis after snake bite or scorpion sting, previous studies in Turkey also found a similar pattern of widespread antibacterial agents use in envenomations.[7,15,16,19,23,24,26] A possible explanation for prophylactic use of systemic antibacterial agents could be the potential for infection due to incisions inflicted by the poisoned patients on the bite or sting sites under non-sterile conditions, as addressed before.[7,23,27] World Health Organisation guidelines for management of snake bites recommend the use of systemic antibacterial prophylaxis in case of tissue breakdown and self-inflicted incisions.[27] The appropriate use of antibacterial agents in envenomation cases should be thoroughly examined in controlled trials to reduce the chance of antibiotic exposure and resistance developing as a result. Public education campaigns could also be organised to prevent the practice of self-incision in envenomations.

## CONCLUSION

We reported that snake and scorpion envenomation were mostly admitted to the ICU with local and/or systemic symptoms for advanced monitoring and observation. Antivenom and antibacterial agent use was common administered treatments. Although life treating emergencies and mortality was uncommon in our study, we think that these patients should be closely followed up in ICU*Limitations*

The inclusion of only envenomation cases admitted to a referral ICU in Sanliurfa can be the strength of this study as this population was representative of the southeastern Turkey as part of the Middle East region where high morbidity is associated with snake or scorpion envenomations. The retrospective nature of the study, reliance only on available medical records and the relatively small study cohort are considered the limitations of our study. However, we were able to study a well-defined and specific group of envenomations and interpret findings to identify unmet needs in the critical management of snake bites and scorpion stings in Turkey.

**Author Contributions:** Conception and design of the study (FTB, BA, TBT, GP, MT, AK); acquisition of the data (FTB, BA, TBT, GP); data analysis (FTB, BA); writing of the manuscript (BA, MT, AK); critical revision of the manuscript (FTB, BA, TBT, GP, MT, AK). All authors read and approved the manuscript.

**Funding and support:** None
**Disclosures:** None.

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