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Research Paper

A Seven-year Epidemiological Study of Snakebite Cases Among Children and Adolescents in South Khorasan, Eastern Iran

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ABSTRACT

Background: This study aims to examine the demographics, risk factors, interventions, and outcomes of pediatric snakebite victims in South Khorasan, Iran. It provides crucial insights for healthcare workers and policymakers. The results can guide future interventions and policies to address this significant public health issue.

Methods: This retrospective study analyzed all children and adolescents with snakebite complaints from 2015 to 2022. Data on age, gender, bite location, clinical and laboratory symptoms, treatment, and outcomes were collected and analyzed.

Results: The prevalence of snakebite was 1.55 per 100000, with 34 cases. The mean age was 9.38±3.91 years. Most patients were men and from rural areas. Snakebites mostly occurred at night, in spring and summer, and involved the lower extremities. Pain was the most common symptom. Coagulation disorder was the most prevalent laboratory finding (76.5%). Antivenom was given to 91.2% of patients. No deaths were reported. One case was compartment syndrome and three cases were gangrene (8.8%). Hospital stay duration showed no significant differences based on gender, residence, season, time to hospital, age group, or treatment type (P>0.05).

Conclusion: Despite the low prevalence, snakebites are a significant health issue for children in South Khorasan, especially in rural areas. The high frequency of coagulopathy underscores the urgent need for early antivenom administration and close monitoring. Providing information about local snake species to health clinics can aid patient management, but swift and effective treatment is the key to reducing the impact of snakebites. These results should serve as a call to action for healthcare professionals, researchers, and policymakers to prioritize early intervention in snakebite cases.

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Introduction

Venomous snake bites pose serious public health issues globally, especially in rural tropical and subtropical areas, leading to significant mortality [1, 2]. The World Health Organization (WHO) reports approximately 5.4 million snake bites annually [2], with global incidence and mortality rates of 0.33 and 69.4 per 100,000, respectively [2]. Asia and Africa have the highest morbidity rates, with Asia's mortality rate at 0.96 per 100,000, followed by Africa at 0.44 per 100,000 [2]. In Iran, healthcare institutions recorded 53 787 snakebite cases from 2002 to 2011, with an annual incidence rate ranging from 4.5 to 9.1 per 100,000 and 67 fatalities [3]. Southern and southwestern Iran experience the highest incidence of snake bites, likely due to the abundance of venomous snakes and the hot, dry climate [3]. Snakes are categorized as poisonous, semi-poisonous, and non-poisonous [4]. About 2900 snake species, with 69 species identified in Iran, including 36 non-venomous, 25 venomous, and eight semi-venomous species [4-6], predominantly found in dry regions [4]. There are approximately 2,900 species of snakes in the world. Iran has 69 identified species, including 36 non-venomous species, 25 venomous species, and eight semi-venomous [4-6].

Children represent 30%-50% of snakebite victims worldwide [7-10] and are more vulnerable due to their greater body surface area, lesser extracellular fluid volume, and limited protein to bind to circulating poisons [7]. They face higher risks of complications, such as pulmonary edema, necrosis, and coagulopathy, often due to delayed medical treatment, higher venom load, and physiological differences [11-13]. Snakebites in children are prevalent in low and middle-income countries with weaker healthcare systems and limited resources [10]. Ensuring access to effective antivenoms, better training for healthcare workers, and preventative measures are crucial to reducing snakebite incidents in children globally [10]. This study aims to analyze snakebite occurrences in children and adolescents in South Khorasan, Iran, over seven years (2015-2022), focusing on epidemiological factors, demographics, clinical presentation, treatment, and outcomes.

Materials and Methods

This descriptive-analytical retrospective study analyzed the records of children and adolescents aged one month to 18 years who visited Vali-Asr Hospital in Birjand City, Iran with snakebite complaints from 2015 to 2022. Collected information included age, gender, residence, bite time and location, clinical symptoms, treatment type, hospitalization duration, treatment outcomes, time to hospital presentation, therapy response, antivenom dose, laboratory test abnormalities, deaths, and causes of death, recorded in a pre-designed checklist. The data were entered into SPSS statistical software version 22.

Statistical analysis

Descriptive data were reported using central and dispersion statistical indices. The Kolmogorov-Smirnov test assessed data normality. Due to non-normal distribution, the Mann-Whitney U, Kruskal-Wallis, chi-squared, and Fisher's exact tests were used for data analysis. A significance level of ≤0.05 was considered appropriate.

The rationale for chosen statistical tests

• Kolmogorov-Smirnov test: Assessed data distribution normality, informing the choice of subsequent tests.

• Mann-Whitney U test: Compared differences between two independent groups (e.g. gender) for non-normal data.

• Kruskal-Wallis test: Compared differences between more than two independent groups (e.g. age groups, seasons) for non-normal data.

• Chi-squared test or Fisher's Exact test: Assessed relationships between categorical variables (e.g. residence, season of bite), with Fisher's exact test used for small sample sizes.

Results

Thirty-four snakebite cases were reported from the beginning of 2015 to the end of 2022; the largest was 12 years in 2021. The average age of the patients was 9.38±3.91 years, ranging from 3 to 18 years. Nineteen of the 34 snakebite cases (55.9%) were men. Most snakebite cases occurred at night, in the spring and summer, and in May and July. The most common anatomical site of the bite was the lower limb, with a frequency of 70.5% (24 individuals). Antivenom was used in 91.2% of the cases (Table 1).

Table 2 presents the clinical and laboratory features of the patients. The predominant symptoms in the individuals under investigation were pain and swelling sequentially. A coagulation disorder was the most prevalent laboratory finding, observed in 76.5% of the patients.

Table 1. Frequency distribution of demographic characteristics and bite characteristics

Characteristics		No. (%)
Gender	Male	19(55.9)
	Female	15(44.1)
Age group (y)	<5	6(17.6)
	5 -10	16(47.1)
	>10	12(35.3)
Residence	Urban	8(23.5)
	Rural	26(76.5)
Season of bite	Spring	15(44.1)
	Summer	15(44.1)
	Autumn and Winter	4(11.8)
Bite location	Upper limb	10(29.4)
	Lower limb	24(70.6)
Years	2015	3(8.8)
	2016	3(8.8)
	2017	5(14.7)
	2018	4(11.8)
	2019	1(2.9)
	2020	5(14.7)
	2021	12(35.3)
	2022	1(2.9)
Time to reach the hospital (h)	<4	13(38.2)
	≥4	21(61.8)

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Antivenom was given in 91% of the cases. The mean dosage of antivenom administered to the children and adolescents under study was 4.80±3.17 units, ranging from 1 to 18. No fatalities were reported among the snakebite patients. Three cases of limb gangrene and one case of compartment syndrome were documented. The average length of hospitalization was 3.08±1.97 days with a range of 1-12 days.

According to the results of the present study, the mean length of hospital stay in children did not differ significantly by age group, gender, place of residence, season of the bite, time to reach the hospital, or anatomical site of the bite (P>0.05). The mean period of hospitalization in children did not vary significantly according to the administration of analgesics, antivenom, antibiotics, and blood products (P>0.05). The hospitalization duration of individuals who received antivenom was significantly higher than those who did not (P<0.05) (Table 3).

Discussion

The prevalence of snakebites in Iran varies due to geography, climate, and the distribution of venomous snakes. Despite South Khorasan's dry, warm climate, its snakebite incidence was low at 1.55 per 100,000 people.

Table 2. Clinical and laboratory characteristics of patients with snakebite

Characteristics		No. (%)
Symptoms	Pain	25(73.5)
	Swelling	22(64.7)
	Localized symptoms (bruising, blisters, erythema)	7(20.6)
	Fever and sweating	7(20.6)
	Abnormal bleeding	5(14.7)
	Respiratory distress	1(2.9)
	Neurological symptoms (seizures, headache, altered consciousness, shock)	7(20.6)
	Gastrointestinal symptoms (nausea and vomiting, diarrhea)	9(26.5)
Laboratory test abnormalities	Leukocytosis	10(29.4)
	Leukopenia	1(2.9)
	Coagulation test abnormalities	26(76.5)
	Abnormal PT	21(61.8)
	Abnormal PTT	11(32.4)
	Abnormal INR	25(73.5)
Treatment types	Analgesics	5(14.7)
	Tetanus toxoid	3(8.8)
	Anti-venom	31(91.2)
	Antibiotics	20(58.8)
	Blood products	9(26.5)
Complications	Limb gangrene	3(8.8)
	Compartment syndrome	1(2.9)

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Snakebites are more frequent in Khuzestan, Hormozgan, Khorasan, Sistan, and Baluchestan provinces [14], where Hormozgan has 31 cases per 100,000 [14], and Kashan, and Isfahan provinces have reported fewer than 2.5 per 100,000 [5]. Factors, such as location, climate, rural areas, occupational risks, and public awareness influence these rates [14, 15], and awareness plays a key role in South Khorasan's low incidence.

In this study, the mean age of children affected by snakebite was 9.38±3.91 years, similar to those in eastern India (10.4 years) and Morocco (10 years) [7, 16]. This age group, especially men, is at higher risk due to increased activity and risk-taking behavior. Men are more commonly bitten [4, 5, 17-22] because they participate more in outdoor and agricultural activities, while cultural factors in some regions reduce female exposure to snakebites [23].

Most patients (76.5%) came from rural areas where agriculture and animal husbandry heighten snakebite risks [17, 19, 20, 24-26]. According to other studies, incidents are more frequent in spring and summer, especially in May and July [5, 17, 24-26] because these months coincide with the farming season and snakes' ectothermic nature [27]. Some studies report higher snakebite rates during rainy seasons due to increased human activity and snakes being displaced from their burrows [23, 24, 28].

Table 3. Comparison of hospitalization time according to the characteristics of snakebite patients

Specifications		Mean±SD	Median (Quartiles)	Z-statistic or χ^2 (Chi-square)	P
Gender	Boy	3.57±2.41	3 (2-4)	1.8	0.08
	Girl	2.46±0.99	2 (2-3)		
Age (y)	<5	3.5±1.97	3 (2.25-4.75)	1.23	0.54
	5-10	2.75±0.93	3 (2-3)		
	>10	3.33±2.90	2.5 (2-3)		
Place of residence	City	2.37±0.74	2.5 (2-3)	1.2	0.22
	Village	3.30±2.18	3 (2-3.25)		
Season of bite	Spring	2.80±1.3	3 (2-3)	0.99	0.80
	Summer	3.53±2.60	3 (2-4)		
	Autumn and winter	2.5±1.00	3 (1.5-3)		
Antivenom usage	Yes	3.22±2.01	3 (2-3)	2.1	0.04
	No	1.66±0.57	2 (1-2)		
Blood product usage	Yes	3.22±1.09	3 (2-3)	1.1	0.29
	No	3.04±2.22	3 (2-3)		
Time to reach the hospital (h)	<4	2.12±0.64	2 (2-2.75)	1.6	0.11
	≥4	3.38±2.15	3 (2-3.25)		
Bite location	Upper limb	1.60±0.51	2 (1-2)	0.13	0.89
	Lower limb	1.62±0.42	2 (1-2)		

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Rainfall attracts snakes due to the abundance of toads and frogs, increasing human-snake encounters [24]. Many bites occur at night, studies in Khorramshahr and Abdanan provinces show that the peaks occur between 6 PM and midnight, and 45% occur between midnight and 6 AM [4]. Another study in southern Iran reported that most bites between midnight and 6 AM [14] are influenced by lifestyle, snake species, and low visibility at night.

In this study, 70.5% (24 individuals) of snakebites occurred on the lower limbs, consistent with results from several other studies [4, 18, 19, 20, 23, 24]. Snake species distribution, environmental factors, occupational habits, and clothing influence bite location. Snakes among vegetation and stones likely contribute to the higher incidence of lower limb bites [4]. Additionally, people often use their lower extremities to investigate objects on the ground, and many lack proper protective gear, such as gloves and boots, during agricultural work [14].

As seen in other studies [18, 23, 24], pain and swelling were the most common symptoms. Venom is usually injected subcutaneously or intramuscularly, causing local tissue damage, and can also be absorbed systemically via lymphatic and blood vessels [27].

A high prevalence of coagulation abnormalities (76.5%) was found, with abnormal prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR), indicating significant hematological complications from envenomation. These disorders which are common in snakebite patients [6, 7, 11, 29-31] result from procoagulant and anticoagulant toxins in the venom, which can cause disseminated intravascular coagulation (DIC) or uncontrolled bleeding [31-33]. Children are more affected than adults due to a higher venom concentration relative to body size, and age-related variations in coagulation factors can worsen these disorders, complicating diagnosis and treatment [7, 8, 11].

In confirmed cases of *Echis carinatus sochureki* bites in northeast Iran, coagulopathy occurred in 40.7% of patients, showing severe hemostatic disturbances from venom containing procoagulants, platelet-activating toxins, and hemorrhages. These cause coagulopathy, thrombocytopenia, vascular damage, and bleeding [29]. Similarly, *Macrovipera lebetina* venom contains phospholipase A2 (PLA2), hyaluronidase, and procoagulant factors V and X activators, contributing to coagulopathy and local tissue damage [29].

In Naik's study, 36.6% of patients had coagulation disorders, lower than our results [28]. This difference may stem from patient age, geographic location, snake species, and sample size variations. Factors, such as proximity to healthcare, community awareness, and prompt antivenom administration also contribute. Pattanaik et al. [7] found coagulation disorders in 4.5% of children treated within 6 hours but 50% when treatment was delayed. The high prevalence in our study highlights the need for early diagnosis and management to prevent life-threatening hemorrhages.

In this study, 91.2% of patients received antivenom, likely due to the region's geography, clinical symptoms, and antivenom availability. Antivenom is a global and regional treatment [8, 34], saving lives and reducing toxin effects when administered early, leading to quicker recovery and shorter hospital stays [35]. Although the specific snake species were not identified, South Khorasan's environment supports various venomous snakes, raising the risk of severe toxicity.

For healthcare providers in Birjand City, strict antivenom guidelines were followed, with an average of 4.80±3.17 vials administered. This dosage contrasts with other studies, such as Mohammadi›s (2.26±0.77 vials) and Indian reports, where over 8-10 vials were used [18, 28, 35]. Variations in dosage result from differences in envenomation severity, regional factors [8], antivenom potency, and snake species [36], as well as the lack of standardized dosing for children, often relying on clinical judgment [35].

Research showed that antivenom doses for children are similar to those for adults because venom volume is not size-dependent [8]. Initial doses can vary from 1 to 30 vials, with additional doses if symptoms persist. This variability reflects adherence to clinical guidelines and the importance of antivenom in reducing snakebite toxicity. Early administration leads to better outcomes and faster recovery. More research is needed to create standardized, evidence-based dosing guidelines for children [8].

The average hospital stay in this study was 3.08±1.97 days, similar to Ndu et al.'s results of 3.2±3.4 days in Nigeria [24]. In Karun County, Iran, most patients stayed 2-3 days, slightly shorter than in our study [6]. In India, stays ranged from 5.6 to 7.2 days [37], while in Sri Lanka, it was 3.5 days [14]. Even without clinical toxicity, patients should be monitored for snakebites for at least 12 hours after hospitalization [12].

The average hospital stay in Birjand City may be shorter than in regions, such as India but is consistent with the 2-3 days reported in Karun City, Iran. Hospitalization duration in South Khorasan is consistent with global standards, though variations across regions make exact comparisons difficult.

This study found no significant variation in hospital stay duration based on gender, residence, season, time to hospital, or age group ($P>0.05$). In contrast, a study in eastern India reported longer stays for children seeking care after 6 hours (7.2 days) compared to 6 hours (4.7 days) [7]. Kumar's study found significant differences based on hospital arrival time, which differs from our results [38].

Hospitalization was longer for patients who received antivenom, indicating more severe envenomation and the need for extended care. However, the moderate overall stay suggests effective treatment protocols. Like Abouyannis' study, patients receiving antivenom had longer hospital stays, likely due to more severe cases [39].

Complications in this study included limb gangrene (8.8%) and compartment syndrome (2.9%). Three patients developed gangrene, and one had compartment syndrome. National Defense University (NDU) research found gangrene in 7.7% of patients [24], while Kumar's study reported 14.46% of children with compartment syndrome [38]. These severe outcomes, often linked to viper bites in Iran [15], highlight the need for prompt treatment to prevent tissue necrosis and long-term disabilities.

No fatalities were reported among the 34 cases, indicating effective medical intervention. This lack of fatalities contrasts with higher mortality rates in other regions, reflecting the success of Birjand's healthcare system. Similarly, Islamian's study in northwest Iran [40] and Mohammadi's research [18] also reported no deaths. In Karun County, Hafezi recorded only three deaths among 287 cases [6]. In comparison, Sri Lanka reported

a 0.16% mortality rate, Bangladesh 16.5% [4], and India 3.8% and 18.8% [3].

Studies showed that younger children, especially those under 5 years, face a higher risk of death from snakebites due to their smaller body mass and greater venom distribution [41, 42]. While the mortality rate among Iranian children is low, it varies by location, snake species, and medical access. The absence of fatalities in this study may be due to prompt medical care, effective treatment, antivenom availability, and encounters with less toxic snake species.

While more information on the population, snake species, and other factors would clarify the causes, the absence of fatalities is a positive outcome, especially compared to higher fatality rates in India and Bangladesh. This outcome suggests that the region's medical treatments and prompt care are effective, aligning with the global high standards in well-administered healthcare systems.

Conclusion

The seven-year study in South Khorasan, Eastern Iran, showed that snakebites primarily affected men in rural areas during spring and summer. Prompt antivenom administration and effective medical interventions resulted in zero fatalities, though complications, such as gangrene and coagulation disorders were observed. The study emphasizes the importance of timely medical care and demonstrates the effectiveness of current treatment protocols in managing snakebites in the region.

Potential biases and limitations

This study had several limitations. Underreporting may have occurred, especially for mild cases where patients did not seek hospital care. Incomplete records could also bias the analysis. The retrospective design introduces recall bias due to reliance on past documentation. Additionally, being limited to one hospital may affect the findings' regional representativeness, and the results may not be generalizable to other areas or age groups.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Birjand University of Medical Sciences (BUMS), Birjand, Iran (Code: IR.BUMS.REC.1401.332).

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Authors' contributions

All authors contributed to the study design, data collection, analysis, and manuscript preparation. They reviewed and approved the final version of the manuscript.

Conflict of interest

The authors declared no conflict of interest.

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