




Original Article

Clinical features and prognosis of severe scorpion envenomation in children

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Abstract **Background:** Scorpionism is endemic and represents a real public health problem in Morocco. The most dangerous arthropod in the central area is *Androctonus mauretanicus* (Am) scorpion. Its venom can be lethal, especially for children. This study aimed to determine a clinico-epidemiological profile of severe scorpion envenomation among children and identify risk factors for mortality.

Methods: This retrospective cohort study included 606 children admitted for severe scorpion envenomation (SSE) from January 2010 to July 2015 in the Pediatric Intensive Care Unit (PICU) of Mohammed VI Teaching Hospital.

Results: The mean age of envenomed children was 6.3 ± 4.2 years. Seventy-four percent of them came from rural settings. Envenomation occurred mostly during the summer months and 78.4% of stings were nocturnal. The time between the sting and evaluation was greater than 2 h in 83% of cases. Bivariate analysis indicated that from 1 to 24 months of age ($P = 0.001$), hyperthermia ($P = 0.022$), episodes of diarrhea ($P < 0.001$), tachycardia ($P < 0.001$), abdominal distention ($P < 0.001$), skin marbling ($P < 0.001$), signs of respiratory distress ($P < 0.001$), irritability ($P < 0.001$), generalized seizures ($P = 0.053$), and Glasgow Coma Score (GCS) of 3 to 9 ($P < 0.001$) were significantly correlated with mortality. On multivariate analysis, diarrhea ($P = 0.007$), skin marbling ($P = 0.006$), and respiratory distress ($P = 0.002$), and GCS 3-9 ($P = 0.007$) were found to be independent risk factors for mortality in our patient population.

Conclusions: Children are at high risk of developing serious complications, even death, from severe scorpion envenomation. Here we identified multiple factors that appear to increase the mortality risk in children after scorpion envenomation, including previously described central nervous system alterations.

Key words *Androctonus mauretanicus*, child, clinico-epidemiological profile, severe scorpion envenomation.

Envenomation from scorpion stings is a substantial public health concern in Asian, Middle Eastern, African, and Latin American countries, with over one million stung people resulting in over 3,000 deaths annually.¹ The pediatric intensive care unit (PICU) of Mohammed VI University Hospital counts around 751 admissions per year, with a mean of 256 ventilated patients and 101 patients admitted for severe scorpion envenomation. Scorpions are endemic to Morocco and scorpion stings are a serious public health issue, especially in central and southern regions of the country, which generally occur in summer and often lead to serious complications.^{2,3}

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The majority of patients stung by scorpions live in rural regions, making it even more challenging for patients to obtain adequate treatment in a timely manner.⁴ The predominantly rural setting of scorpion stings is concerning due to the general lower education level and significant challenges to access of appropriate care, both due to geographically isolated locations, insufficient healthcare in rural settings, and a lack of proper education about this condition in local healthcare workers.

The type and severity of symptoms depends on the species of scorpion, the amount of venom injected, and the age and health of the victim. *Androctonus mauretanicus* (Am), one of the most dangerous scorpions with the most toxic venoms of the Buthidae family, is responsible for almost human deaths due to scorpion stings in Morocco (Fig. 1).⁵

Scorpion stings can cause a variety of symptoms ranging from local pain and inflammation to grave tissue damage.



Fig. 1 *Androctonus mauretanicus* found in the southern regions of Morocco. [Colour figure can be viewed at wileyonlinelibrary.com]

Though 95% of scorpion stings cause only local manifestations, severe cases can be life-threatening with autonomic nervous system involvement and cardio-pulmonary failure, leading to death in the most severe cases.⁶ Increased severity of symptoms is found when the sting occurs in highly vascularized areas such as the trunk, head, or neck, and when children are stung.

The pediatric population is the most commonly affected and also at the highest risk of death. The annual victim count is estimated at 30–50 000 per year, and according to the Moroccan Anti-Poison Center (MAPC), the incidence of these scorpion stings represent 30–50%, of all reported poisonings, putting it at the top of the Moroccan list of all poisonings and intoxications.^{2,7}

While envenomation occurs after scorpion stings only approximately 21% of the time, it is imperative to identify those who have been envenomed as symptoms may be severe, particularly in children. The overall case fatality rate is 1.5%, but 90% of these deaths occur in children less than 15 years old.² The increased mortality rate seen in children may be due to several factors including immaturity of physiological systems resulting in decreased defenses against major insults, higher ratio of injected venom to bodyweight, and likely an immature blood-brain barrier (BBB), leading to more direct but still controversial neurotoxic effects.^{8–11}

Appropriate antivenom has been shown to prevent mortality and decrease myotoxic and neurotoxic effects during *in vitro* studies.³ It is not clear if antivenom decreases mortality *in vivo*, but has been demonstrated to decrease duration and severity of symptoms.¹² However, antivenom has many challenges: it is not widely available, especially in developing countries where it is needed most; it requires special storage, it has a short shelf life, and requires critical care capabilities in case of an anaphylactic reaction.¹³

This study presents an epidemiological overview of dangerous scorpion stings and their impact on childhood health and a clinical profile analysis of severe scorpion envenomation (SSE) with predictive factors of poor outcomes in the pediatric population of Morocco.

Methods

Data collection

This was a collaborative study between the PICU of Mohammed VI Teaching Hospital of Marrakech and the Pharmacology, Neurobiology and Behavior Lab of Semlalia Faculty of Sciences.

A retrospective review was done of the charts of all patients below the age of 15 years who were admitted to the PICU and who developed SSE or Class III as defined in accordance with the consensual classification based on clinical consequences of scorpion stings that was proposed by a panel of international experts.¹⁴ In other words, children who presented at least one life-threatening sign and / or symptom relating to respiratory, cardiac and / or central nervous system failure.¹¹ The inclusion period was between January 2010 and July 2015. Patient demographics and clinical features were recorded, including age (divided into three groups, from birth to 2 years old, >2 to 5 years old, and above 5 to 15 years old), gender, past medical history, regional origin, number of stings, body site, time since sting, referral from other health facilities, symptoms on admission, neurological or behavioral changes, Glasgow Coma Score (GCS), categorized into three groups (3–9, 10–14, and 15), and treatments received. The study was approved by the Medical School of Marrakech local ethics committee.

Statistical analysis

A bivariate analysis was performed to study the various clinical factors associated with mortality using the Student *t*-test or the Mann–Whitney *U*-test for non-parametric variables, as applicable. Quantitative items were categorized and the χ^2 test was used for qualitative variables. Variables with a *P*-value of less than 0.05 were then entered into a multivariate logistic regression analysis. A final *P*-value of <0.05 was considered

Table 1 The mean frequency of symptoms developed after SSE (n=606)

Symptoms	Alive 559 (92%)	Deceased 47 (8%)	Total 606 (100%)
General			
Hyperthermia	203 (36.3%)	25 (53.2%)	228 (37.6%)
Sweating	483 (86.4%)	37 (78.7%)	520 (85.8%)
Priapism	196 (35%)	21 (44.7%)	217 (35.8%)
Digestive signs			
Nausea / vomiting	488 (87.3%)	41 (87.2%)	529 (87.3%)
Abdominal pain	217 (38.8%)	21 (44.7%)	238 (39.3%)
Diarrhea	15 (2.7%)	12 (25.5%)	27 (4.5%)
Abdominal distension	27 (4.8%)	11 (23.4%)	38 (6.3%)
Hemodynamic instability			
Tachycardia	263 (47%)	42 (89.4%)	305 (50.3%)
Thready pulse	28 (5%)	24 (51.1%)	52 (8.6%)
Prolonged capillary refill time	201 (35.9%)	45 (95.7%)	246 (40.6%)
Mottled skin	23 (4.1%)	25 (53.2%)	48 (7.9%)
Cyanosis and/or cold extremities	542 (96.9%)	47 (100%)	589 (97.2%)
Pulmonary symptoms			
Crepitant crackles	84 (15%)	32 (68.1%)	116 (19.1%)
Tachypnea and retractions	23 (4.1%)	29 (61.7%)	52 (8.6%)
Neurologic symptoms			
Irritability	47 (8.4%)	21 (44.7%)	68 (11.2%)
Seizures	13 (2.3%)	3 (6.4%)	16 (2.6%)
Generalized	11 (1.9%)	3 (6.4%)	14 (2.3%)
Partial	2 (0.3%)	0 (0%)	2 (0.3%)
Altered mental status (GCS < 15)	112 (20%)	41 (87.2%)	153 (25.1%)
Behavioral changes	181 (32.4%)	32 (68.1%)	213 (35.1%)
Neurological deficits	1 (0.2%)	0 (0%)	1 (0.2%)

GCS, Glasgow Coma Score; SSE, Severe Scorpion Envenomation

significant. Analysis was performed using the IBM SPSS (Statistical Package for the Social Sciences) Statistics for Windows, Version 19.0. Released by IBM Corp in 2010, Armonk, NY, USA.

Results

Of the 1225 children admitted to the University Hospital for scorpion envenomation, 606 suffered from SSE and were enrolled in the study. They had a mean age of 6.3 ± 4.2 years (ranging from 2.5 months to 15 years), with 62% of the population being pre-school aged children (less than 7 years old). The male to female ratio was 1.56:1.

The average annual recruitment was 96 severely envenomed children per year. Among them, 30% came from the Al Haouz region, followed by Chichaoua, Rehamna, Marrakech, El Kelaa, and Essaouira (24%, 19%, 15%, 10%, and 2%, respectively) (Fig. 2). The majority of cases, nearly 74%, came from rural settings; 85.7% of stings occurred during the summer months (June to September) and 78.4% occurred at night. Close relatives who witnessed the envenoming event have in almost cases (95%) identified the venomous arthropod as Am species when shown an indicative photo. Stings were most frequently located

in the extremities, with 54.8% occurring on the hands or feet. In 83% of patients, the time between the sting and administration of appropriate care (systematic and parenteral administration of dobutamine as dictated by the national protocol in case of SSE or Class III) was more than 2 h. None of the envenomed children received antivenom.

The overall mortality rate was about 8% ($N = 47$). The majority of deaths were due to refractory cardiogenic shock, multiorgan failure or ischemic cerebrovascular accidents. The mean hospital stay of patients who survived was 25.9 ± 35.4 days (range 4–282) while the average stay for those who died was 56.4 ± 92.8 days (range 0–576). Upon admission, neurological impairment was found in one-third of cases. Other symptoms are detailed in Table 1.

On bivariate analysis, age of 1–24 months ($P = 0.001$), fever ($P = 0.022$), diarrhea ($P < 0.001$), tachycardia ($P < 0.001$), abdominal distention ($P < 0.001$), skin marbling ($P < 0.001$), respiratory distress ($P < 0.001$), irritability ($P < 0.001$), generalized seizures ($P = 0.053$), and GCS 3–9 ($P < 0.001$) were predictors of mortality. On multivariate analysis, episodes of diarrhea (OR, 0.20 [95%CI: 0.06–0.63], $P = 0.007$), mottled skin (OR, 0.24 [95%CI: 0.09–0.70], $P = 0.006$), signs of respiratory distress (OR, 0.20 [95%CI: 0.07–0.60], $P = 0.002$), and GCS 3–9 (OR, 9.2 [95%CI: 1.9–46], $P = 0.007$) were found to be independent risk factors for mortality in children presenting with SSE (Table 2).

Discussion

Scorpion envenomation is common in rural regions. The venom distribution in the extravascular compartment is fast, explaining the early appearance of the symptoms. Three classes of scorpion envenomation of increasing severity can be distinguished. Class I corresponds to a benign envenomation: pain is immediate, intense, and local with paresthesia at the site of the sting. Class II presents with general signs such as fever, sweating and / or priapism; digestive signs such as nausea and vomiting, abdominal pain, diarrhea and / or abdominal distension; along with hypertension, tachycardia and / or agitation. Class III corresponds to a severe envenomation, and is potentially lethal. At this stage, the consequences are cardiac, respiratory and / or neurological distress¹⁴ (Table 1).

As far as we are aware, this work is one of the largest observational studies, exclusively comprising children admitted to PICU for SSE. In accordance with the above data, most studies report that the majority of scorpion stings occur in the summer and at night time.^{15–17} Between the years 1999 to 2008, the lethality of those envenomed was reported by the MAPC to be 2.7–7.1%, with up to 83% of deaths in children less than 15 years old.^{15,16,18}

Alternatively, in the USA, only one death of a child from scorpion sting was reported in the literature from 1970 to 2013. This disparity, compared to our findings in Morocco, is likely to be due to the strong supportive therapy with aggressive airway management, as well as the lower incidence of stings, with only one deadly scorpion found in few southern

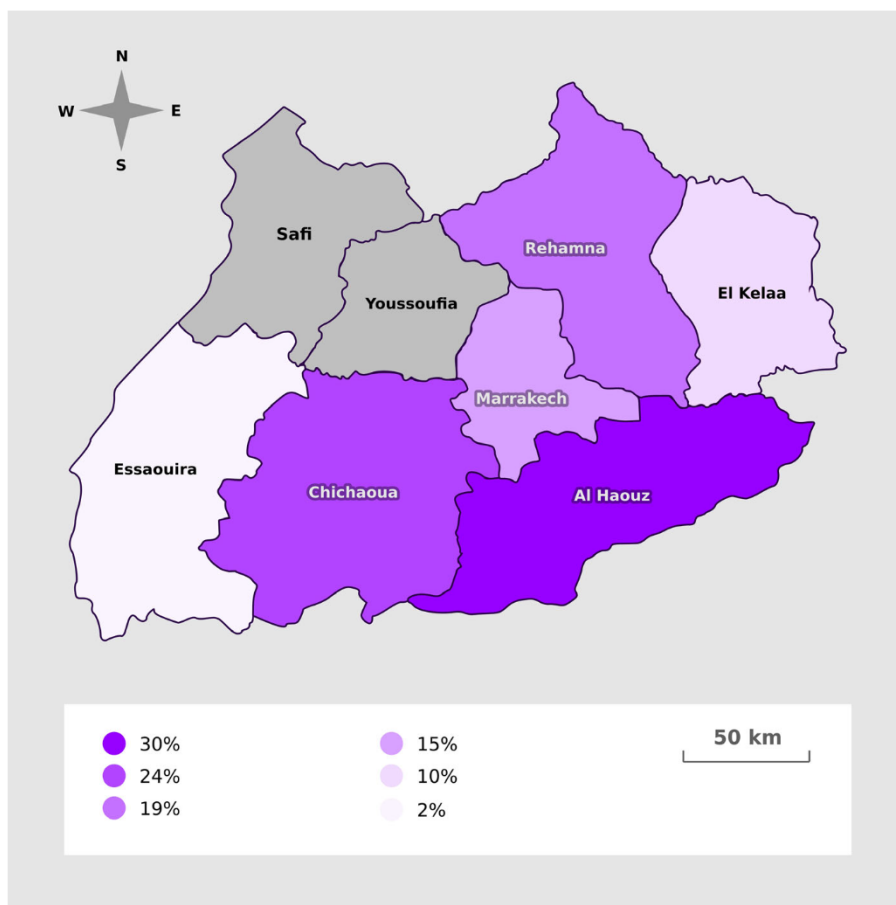


Fig. 2 Geographical distribution of Severe Scorpion Envenomation in Marrakech-Tensift-Al Haouz region. (●), 30%; (●), 24%; (●), 19%; (●), 15%; (●), 10%; (●), 2%. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 2 Bivariate and multivariate analysis of clinical features of severely envenomed children admitted to PICU (n=606)

Variable	Univariate analysis			Reference category	Multivariate analysis		
	P-value	OR	95% CI		OR	P-value	95% CI
Age in years							
(2–5)	0.001			(0–2)	0.4	0.08	0.13–1.1
(5–15)	0.001				0.76	0.06	0.24–1.15
Fever	0.02	1.99	1.1–3.62		0.87	0.07	0.31–5.4
Diarrhea	<0.001	12.43	5.41–28.59		0.2	0.01	0.06–0.63
Tachycardia	<0.001	9.45	3.69–24.25		0.7	0.56	0.22–2.3
Abdominal distension	<0.001	6.02	2.76–13.11		1.8	0.5	0.43–7.26
Mottled skin	<0.001	26.48	13.03–53.80		0.24	0.006	0.09–0.7
Signs of respiratory distress	<0.001	37.55	18.25–77.22		0.2	0.002	0.07–0.6
Irritability	<0.001	8.8	4.6–16.82		0.5	0.2	0.15–1.33
Behavioral changes	<0.001	4.45	2.35–8.44		1.45	0.5	0.5–4.09
GCS							
(10–14)	<0.001			(3–9)	9.2	0.007	1.9–46
15	<0.001				12.3	0.0003	2.2–23

CI, confidence interval; GCS, Glasgow Coma Score; OR, odds ratio; SSE, Severe Scorpion Envenomation. Bold values are used to emphasize on their significance in multivariate analysis.

states, while scorpions with deadly venom are found throughout the country of current study.^{12,19}

In Tunisia, approximately 2.5% of stung children required hospitalization, and 1% of them died from scorpion

envenomation. In a retrospective review of 685 children admitted for scorpion sting between 1990 and 2002, 84.7% had neurologic manifestations, 39.3% required ventilation, and 8.9% died. It is of note that 56.6% of the patients had received

antivenom prior to admission.²⁰ In a review of scorpion stings occurring in the Brazilian Amazon, 14.8% of patients were under the age of 10 and the overall fatality for the 2,120 cases studied was 0.3%, with a 1.3% fatality rate in children under the age of 10. Only 4.6% of patients in this series were classified as severe.²¹

Additionally, while 22% of the patients hospitalized for scorpion stings in Sri Lanka were children under the age of 12 and 8.2% of those examined in Iran were under the age of 10, no deaths were seen in these series, potentially indicating the serious toxicity of Moroccan Am scorpions.^{22,23} Compared to the 4.74% mortality seen in a study of patients from the Zagora oasis,¹⁷ the overall mortality rate was higher in our population, possibly due to our hospital being a tertiary referral center for a large region of the country and our study including only severely envenomed children.

The delay in seeking emergent treatment and in referring victims to specific healthcare facilities must contribute to most of rural deaths. A study from Morocco identified time to ICU admission of over 5 h after the sting as the only significant risk factor for death in the population studied.²⁴ Children are more susceptible to scorpion envenomation, and the clinical manifestations of envenomation can be more severe in children and result in multiorgan failure and death.²⁵ In another study reported by Bahloul *et al.*, factors associated with a poor prognosis were found to be GCS <8, pulmonary edema, or cardiogenic shock upon admission.²⁰ Some authors suggest that pulmonary edema in severe scorpion envenomation is cardiac in origin, as the venom is a powerful arrhythmogenic agent, it stimulates the autonomic sympathetic nervous system and adrenals, and induces dramatic hemodynamic increases in the left ventricular systolic and diastolic pressure, pulmonary and systemic arterial pressures and left ventricular contractility. Heart failure is most probably the result of the interaction of several mechanisms that include a catecholamine-induced decrease in left ventricular compliance and increased impedance to left ventricular emptying and cardiac arrhythmias, all of which may impede left ventricular filling.²⁶

In Brazil, age less than 10 years and stings occurring in rural or southern regions of the state were independent risk factors for developing severe symptoms.²¹ Our study details clinical risk factors for death, corroborating what were previously reported, such as signs of respiratory distress and low GCS score, in children who present with severe scorpion envenomation. At the same time it adds the newest ones including episodes of diarrhea and skin marbling.

To mediate some of these challenges, a score was developed to assist in identifying patients who require hospitalization with a sensitivity of 89.2% using only symptoms easily identified upon presentation without requiring biological analysis or calculations. According to this scoring paradigm, the most important factors determining whether a patient requires hospitalization is priapism, followed by vomiting, systolic blood pressure above 160, and steroid administration before arrival to the emergency department.⁴ We recommend that this scoring method be utilized in rural clinics to decrease the time

wasted on observation of cases that eventually will need to be admitted. It is imperative that health-care workers are trained in identifying severe envenomation and those most likely to require hospitalization, as rapid intervention appears to be key in the treatment of scorpion envenomation.

Limitations

Restricting the inclusion criteria to only severely envenomed children could limit the generalizability of the risk factors for all patients envenomed. However, we believe the results are still of value in clinical practice as severely envenomed children are those most at risk for rapid deterioration and may benefit most from the interventions discussed here. The low incidence of death also limits the statistical analysis that can be performed.

Conclusion

Children in Morocco, especially those living in rural settings, are at high risk of serious complications and death from scorpion stings. It is of critical importance to increase education and access to appropriate medical care in isolated regions to ensure the safety and protection of our country's children. This study found that episodes of diarrhea, marbling of the skin, signs of respiratory distress, and a low GCS on admission to the ICU are significant independent risk factors for mortality after sting from the Am scorpion commonly found in Morocco. These symptoms, not previously identified, can help inform physicians of patients most at risk for severe sequelae and guide therapeutic interventions to prevent poor outcomes.

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Disclosure

The authors declare no conflicts of interest.

Informed consent

The data were old, de-identified and anonymized, then we did not need consents.

Human rights

This is a retrospective study and all human rights were well respected.

Author contributions

H.R. designed the study, collected and analyzed the data and drafted the manuscript. S.B. and M.B. analyzed the samples and gave technical support. Y.M. and S.Y. provided

conceptual advice. M.E.S. helped in both writing the paper and data analysis. All authors read and approved the final manuscript.

Data availability statement

The data were extracted from the Clinical Data Analysis and Patient Record System of the Mother and Child Hospital.

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