Scorpion Envenomation Among Children: Clinical Manifestations and Outcome
(Analysis of 685 Cases)

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Abstract. Our objective was to characterize both epidemiologically and clinically manifestations after severe scorpion envenomation and to define simple factors indicative of poor prognosis in children. We performed a retrospective study over 13 years (1990–2002) in the medical intensive care unit (ICU) of a university hospital (Sfax-Tunisia). The diagnosis of scorpion envenomation was based on a history of scorpion sting. The medical records of 685 children aged less than 16 years who were admitted for a scorpion sting were analyzed. There were 558 patients (81.5%) in the grade III group (with cardiogenic shock and/or pulmonary edema or severe neurological manifestation [coma and/or convulsion]) and 127 patients (18.5%) in the grade II group (with systemic manifestations). In this study, 434 patients (63.4%) had a pulmonary edema, and 80 patients had a cardiogenic shock; neurological manifestations were observed in 580 patients (84.7%), 555 patients (81%) developed systemic inflammatory response syndrome (SIRS), and 552 patients (80.6%) developed multi-organ failure. By the end of the stay in the ICU, evolution was marked by the death in 61 patients (8.9%). A multivariate analysis found the following factors to be correlated with a poor outcome: coma with Glasgow coma score ≤ 8/15 (odds ratio [OR] = 1.3), pulmonary edema (OR = 2.3), and cardiogenic shock (OR = 1.7). In addition, a significant association was found between the development of SIRS and heart failure. Moreover, a temperature > 39°C was associated with the presence of pulmonary edema, with a sensitivity at 20.6%, a specificity at 94.4%, and a positive predictive value at 91.7%. Finally, blood sugar levels above 15 mmol/L were significantly associated with a heart failure. In children admitted for severe scorpion envenomation, coma with Glasgow coma score ≤ 8/15, pulmonary edema, and cardiogenic shock were associated with a poor outcome. The presence of SIRS, a temperature > 39°C, and blood sugar levels above 15 mmol/L were associated with heart failure.

INTRODUCTION

The epidemiology of the scorpionism in the world is poorly known.¹ Scorpion stings occur on all five continents. However, scorpion stings are more common in some areas, and there is considerable geographic variation in both the incidence and severity.² In Tunisia, almost 40,000 stings are recorded per year.²,³ Around 1,000 individuals have systemic manifestations requiring hospitalization, and about 10 patients eventually die.²,³ The incidence has continued at a high level (1,465 annual scorpion stings per 100,000 inhabitants), but the mortality has decreased dramatically thanks to better management, particularly, shorter period between the time of the sting and medical consultation.²,³ In the governorship of Sfax, the annual incidence is 600 scorpion stings per 100,000 inhabitants, and the annual mortality was (between 1980 and 1990) at 2.83 per 100,000 inhabitants.⁴ In our country, there is a large number of scorpion species. A sample of 132 scorpions collected in the Sfax area (south Tunisia) has shown 70% Androctonus australus; the remaining 30% were Butus occitanus and Scorpio maurus. A. aeneus is always seldom encountered. In some other samples coming from different regions of Tunisia, it was regularly collected but constituted 1% or 2% of the samples.⁴ Nevertheless, in our country, the severe forms of scorpion envenomation requiring intensive care unit (ICU) admission result usually from a sting by one of two species: A. australus and B. occitanus.¹ These two endemic species in south Tunisia are venomous.²,³ The scorpion venoms contain some toxins better known for the buthoids (one family, Buthidae) than for the chaetoids (the five other families), whose venoms are less dangerous for humans.¹ These toxins are small basic proteins containing about 65 amino acids that have a selective activity on mammals or intervertebrates. The scorpion venom has essentially neuromuscular and cardiovascular toxic effects. They are poorly equipped with enzymes, especially the Buthid venom.⁴,⁵

In our country, scorpion envenomation is more observed in middle and south Tunisia (rural areas = endemic areas). In the past (before 1995), all severe forms of scorpion envenomation were transferred to a reference center of scorpion envenomation (ICU of Habib Bourguiba University Hospital, Sfax, Tunisia). In endemic Tunisian areas, most patients live more than 50 km from the nearest facility offering intensive care. Approximately more than 2 hours are needed to reach the district hospital. Tunisian heath authorities began to recognize the importance of the problem and the need for emergent intervention. They understood that the primary health-care system at the district and subdistrict levels needs strengthening to provide adequate medical services. During the past few years, projects were designed to upgrade some district hospitals, and several ICUs were created. As a consequence, currently, severe forms of scorpion envenomation are now admitted and treated in ICUs of rural hospitals, and mortality decreased from 5.5 to 1.6 per 100,000 inhabitants within a decade (between 1990 and 2000).⁴ The correlation between young age and severity of clinical manifestations after scorpion envenomation is well-established.²,⁴ In fact, the signs and symptoms of envenomation are usually more severe in children, especially younger ones. Multiple organ failure (MOF) among scorpion–envenomed children has been reported by many investigators.⁷,⁸ Moreover, cardiorespiratory manifestations, mainly cardiogenic shock and pulmonary edema, are more frequent in children.⁹ For these reasons, evaluation of the severity of the envenomation, mainly in children, is essential to establish the prognosis and institute adequate treatments. The aim of the present study was to characterize the
SCORPION ENVENOMATION AMONG CHILDREN

epidemiological and clinical features of scorpion envenomation and define simple predictive factors that can be used in routine practice in the ICUs to indicate poor prognosis in scorpion-envenomated children in the Sfax area of south Tunisia.

MATERIALS AND METHODS

Patients. We retrospectively included all patients aged less than 16 years admitted for scorpion envenomation over a period of 13 years (1990–2002) in the 22-bed ICU of our university hospital. The diagnosis of scorpion envenomation was based on a history of scorpion sting.

Methods. The patient’s medical records were retrospectively reviewed, and the following data were collected: geographical distribution, age, sex, vital signs (heart rate, respiratory rate, systolic and diastolic blood pressure), body temperature in degrees Celsius (temp), Glasgow coma-scale score (GCS), use of mechanical ventilation, use of inotropic drugs, presence of shock, cardiac arrest, fluid intake volume, and urinary output. Tachycardia was defined by a heart rate > 120 beats/minute, and bradycardia was defined by heart rate < 70 beats/minute.

For each patient, a pediatric risk of mortality score (PRISM) was calculated within 24 hours after ICU admission. The gastrointestinal manifestations were assessed at any time after scorpion envenomation. Moreover, we determined, for each patient, the duration of ICU stay and the mode of ICU exit (home or transfer to another hospital unit).

The neurological manifestations were also assessed: sweating, priapism, coma, convulsions, and agitation. Finally, brain computed tomography (CT)-scan results were analyzed (if the study was performed). Biochemical parameters were measured on admission and during the ICU stay (arterial blood gases and acid-base state, serum glucose, sodium levels, etc.).

The chest roentgenograms performed on admission and throughout the hospitalization period were reviewed. A medical committee of five physicians of our ICU retrospectively examined all the available data to classify patients according to the presence of pulmonary edema at admission. The diagnosis of pulmonary edema was based on the presence of clinical and radiological features of cardiogenic pulmonary edema and the presence of arterial hypoxemia. The medical committee particularly took into account the presence of signs of respiratory distress (tachypnea and inspiratory retraction of intercostals spaces) and the presence of lung crackles on auscultation of one or both lungs. In addition, the medical committee looked for signs of interstitial and/or alveolar pulmonary edema on the chest roentgenograms. In patients receiving mechanical ventilation, arterial hypoxemia was defined as a PaO₂/FiO₂ ratio < 300. The response to treatment of the clinical, radiological, and gas-exchange abnormalities was also taken into account for the diagnosis of pulmonary edema.

We stratified patients into two grades of severity at baseline according to the absence or presence of systemic manifestations. Grade II included patients with systemic manifestations, and grade III included patients with cardiorespiratory manifestations, mainly cardiogenic shock and pulmonary edema or severe neurological manifestations (coma and/or convulsions). This classification is currently recommended by the Tunisian health ministry and is used in clinical practice. In our institution, we typically give dobutamine if the clinical characteristics of the patient suggest pulmonary edema, because it was previously shown that scorpion envenomation can result in pulmonary edema secondary to acute left ventricular failure and dobutamine was shown to be efficacious to improve cardiac function in this specific condition. Organ failures, such as neurological, cardiac, respiratory, hematological, renal, and liver failure, were noted in each patient. Moreover, the presence of systemic inflammatory response syndrome (SIRS) was also assessed on admission and during ICU stay.

STATISTICS

The characteristics of survivors and non-survivors were analyzed by the χ² test. Continuous variables were expressed as means ± standard deviation (SD), and the subgroups were compared by Student t test. Risk factors were evaluated in univariate analysis and multivariate analysis by a multiple logistic stepwise regression procedure. Odds ratios (OR) were estimated from the b coefficients obtained, with respective 95% confidence intervals (CI 95%). For comparable data, a P value less than 0.05 was considered statistically significant.

The value of body temperature and blood glucose level to predict the presence of pulmonary edema and the value of PRISM score to predict mortality were analyzed using receiver operating characteristic (ROC) curves. The area under the curve, which was estimated by the method of Hanley and McNeill, provides a measure of overall diagnostic accuracy of the test. The optimal value for the calculation of positive and negative predictive values was obtained from the ROC analysis.

RESULTS

During the study period, 685 children were admitted for a scorpion sting, and their medical records were analyzed. As shown in Figure 1, the number of stung children clearly decreased from 1990 to 2002. There were 558 patients (81.5%) in the grade III group and 127 patients (18.5%) in the grade II group. Scorpion envenomation is more frequent in the summer; indeed, 81.7% of our patients were admitted between June and September (Figure 2).

The mean age (±SD) was 5.9 ± 3.9 years, ranging from 0.5 to 15 years. The majority of patients were less than 5 years of age (56.7%) (Figure 3). However, only nine (1.3%) patients had one or several pathological antecedents (comorbid conditions). Of all patients, 41% were from Sfax city or its delegations. However, a significant number of patients (59%) were referred to us from outside hospitals from other southern

Figure 1. Number of sting patients admitted into the ICU each year.
Tunisia cities (Figure 4). The site of sting was available in 552 (80.5%) children. The frequency of stings in feet (60.4%) and hands (12.3%) was greater than those on the chest (5.5%) and head (2.3%). In our study, local inflammation was not observed in all patients. Indeed, the stings of Tunisian scorpions typically do not cause local signs.

Body temperature (°C) was measured for 679 patients; it was, on average, 37.8 ± 1.2°C, ranging from 35°C to 42°C. Hyperthermia (>37.8°C) was observed in 351 patients (51.2%), and hypothermia was observed in 59 patients (8.6%). Table 1 shows the frequency of each systemic manifestation in our study. The systolic blood pressure was, on average, 87 ± 21 mmHg. The mean heart rate was at 134.7 ± 22.9 beats/minute. An electrocardiogram was performed in 682 patients (99%). The most observed abnormalities were sinus tachycardia (>120/minute) in 678 patients (98.9%), and T-wave changes were observed in 130 (9%) patients. Other electrocardiography (ECG) abnormalities were also observed, including ST segment depression or elevation observed in 94 (13.7%) patients and sinus bradycardia in 1 (0.3%) patient. Moreover, in three patients who underwent echocardiography, the cardiogenic nature of the pulmonary edema was confirmed by a low value of left ventricular ejection fraction (less than 40%). Moreover, myocardial perfusion scintigraphy (99mTc scintigraphy) coupled with radionuclide ventriculography (99mTc) that was performed in three patients showed evidence of myocardial hypoperfusion in all cases, with a radionuclide ventriculography abnormal with a low value (less than 45%) of left ventricular ejection fraction (LVEF) in all patients.

Five hundred seventeen patients (75.5%) had respiratory manifestations. The mean respiratory rate was at 37 ± 11.4/minute, and 4.6 patients (59.3%) had a tachypnea with a respiratory rate more than 30/minute; 434 (63.4%) had pulmonary edema. Moreover, 269 children (39.3%) required mechanical ventilation during a mean time at 1.2 days. Table 1 showed the frequency of each respiratory manifestation. In this study, 580 patients (84.7%) had neurological manifestations. A consciousness abnormality (GCS ≤ 14) was observed in 177 (25.8%) patients; 123 (18%) of these patients had coma (GCS ≤ 12), whereas 52 patients (7%) developed convulsions. Other signs were also noted, such as agitation in 558 (81.5%) patients (Table 1). A CT scan of the brain was performed in nine patients; cerebral edema and/or brain ischemia were observed in seven patients.

In this study, 507 patients (74%) had gastrointestinal signs. Nausea was observed in five (0.7%) patients, vomiting was seen in 499 (72.8%) patients, and diarrhea was seen in 36 (5.3%) patients. The mortality was significantly higher in patients presenting diarrhea ($P = 0.023$). According to the absence or presence of systemic manifestations, there were 558 patients (81.5%) in the grade III group and 127 patients (18.5%) in the grade II group. The time between sting and admission was recorded in 618 patients. It was, on average, 5 ± 4.27 hours (range = 1–48 hours); time was shorter than 120 minutes in 18% of patients. As shown in Table 2, pulmonary edema, coma, use of catecholamine, and death are less frequently observed in the subgroup with a shorter interval (<2 hours) from the time of the sting until medical consultation. The patients included in the study were seriously ill. In fact, the mean PRISM score on admission was at 21.5 ± 12.6 points; it was above 30 in 29.5% of patients. Moreover, SIRS was observed in 555 patients (81%), and 552 patients (80.6%) developed organ failure in at least one organ. Cardiac failure was observed in 542 (79.1%) patients, respiratory failure was observed in 444 (64.8%) patients, neurological signs and symptoms were observed in 25 (3.6%) patients, renal failure was observed in 13 (1.9%) patients, and hematologic or hepatic failure was observed in 7 (1%) patients. Moreover, most patients (64.7%) had organ failure in more than two organs (Table 3). On admission, 388 patients (56.6%) had received scorpion anti-venom. During their ICU stay, 269 patients (36%) developed respiratory distress requiring mechanical ventilation, and 514 patients (75%) had a pulmonary edema and/or cardiogenic shock requiring the use of inotropic agent (usually dobutamine). Finally, corticosteroids were used in 594 patients (86.73%).

At the end of the ICU stay, the clinical course was marked by the improvement of 624 patients (91.1%), whereas 61 patients (8.9%) died. Univariate analysis showed that high PRISM score on admission ($P < 0.001$), presence of shock and/or...
pulmonary edema ($P < 0.001$), high value of serum glucose ($P < 0.001$), coma ($P = 0.01$), bilateral mydriasis ($P < 0.001$), fever ($P = 0.01$), use of mechanical ventilation ($P < 0.001$), use of scorpion anti-venom ($P < 0.001$), and diarrhea ($P = 0.023$) were associated with mortality (Table 4). The multivariate analysis showed that factors associated with a poor prognosis were coma with GCS $\leq 8$ (OR = 1.3; 95% CI = 1.06–3.40), pulmonary edema (OR = 2.3; 95% CI = 1.56–7.30), and cardiogenic shock (OR = 1.7; 95% CI = 1.33–4.30).

A significant association was found between PRISM score and mortality rate (42.7 versus 19.4; $P < 0.001$). This model had a high discriminative power, with an area under the ROC curve at 0.93. Moreover, the presence of cardiac, respiratory, neurological, renal, hematologic, or hepatic failure was

<table>
<thead>
<tr>
<th>Parameters</th>
<th>All patients (685 patients)</th>
<th>Group 1 (388 patients)</th>
<th>Group 2 (186 patients)</th>
<th>Group 3 (111 patients)</th>
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<td>Systemic manifestations</td>
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<td>Sweating</td>
<td>537 (78.4%)</td>
<td>296</td>
<td>146</td>
<td>95</td>
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<td>Agitation</td>
<td>558 (81.5%)</td>
<td>337</td>
<td>143</td>
<td>78</td>
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<tr>
<td>Priapism</td>
<td>320 (80.2%)</td>
<td>188</td>
<td>79</td>
<td>54</td>
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<tr>
<td>Shiver</td>
<td>47 (6.9%)</td>
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<td>21</td>
<td>18</td>
</tr>
<tr>
<td>Vomiting</td>
<td>499 (72.8%)</td>
<td>281</td>
<td>134</td>
<td>84</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>36 (5.3%)</td>
<td>25</td>
<td>9</td>
<td>2</td>
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<tr>
<td>Cardio respiratory manifestations</td>
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<tr>
<td>Tachypnea</td>
<td>406 (59.3%)</td>
<td>249</td>
<td>100</td>
<td>57</td>
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<tr>
<td>Cyanosis</td>
<td>181 (26.4%)</td>
<td>104</td>
<td>48</td>
<td>29</td>
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<tr>
<td>LC on auscultation</td>
<td>446 (65%)</td>
<td>242</td>
<td>124</td>
<td>80</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>181 (26.4%)</td>
<td>104</td>
<td>48</td>
<td>29</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>434 (63.4%)</td>
<td>239</td>
<td>115</td>
<td>80</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>87 ± 21</td>
<td>82 ± 22</td>
<td>87 ± 18</td>
<td>93 ± 22</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>56 ± 15</td>
<td>52 ± 16</td>
<td>56 ± 10</td>
<td>59 ± 17</td>
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<tr>
<td>Neurological manifestations</td>
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<tr>
<td>Agitation</td>
<td>558 (81.5%)</td>
<td>337</td>
<td>143</td>
<td>78</td>
</tr>
<tr>
<td>Squint</td>
<td>110 (16%)</td>
<td>80</td>
<td>21</td>
<td>9</td>
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<tr>
<td>Bilateral myosis</td>
<td>39 (5.7%)</td>
<td>24</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Bilateral mydriasis</td>
<td>14 (2%)</td>
<td>7</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Anisocoria</td>
<td>4 (0.6%)</td>
<td>2</td>
<td>2</td>
<td>0</td>
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<tr>
<td>Coma</td>
<td>123 (18%)</td>
<td>82</td>
<td>29</td>
<td>12</td>
</tr>
<tr>
<td>Convolutions</td>
<td>52 (8%)</td>
<td>40</td>
<td>9</td>
<td>3</td>
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<td>Treatment and outcome</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Use of inotrope</td>
<td>514 (75%)</td>
<td>291</td>
<td>128</td>
<td>95</td>
</tr>
<tr>
<td>MV</td>
<td>269 (39%)</td>
<td>145</td>
<td>68</td>
<td>56</td>
</tr>
<tr>
<td>Use of corticoids</td>
<td>594 (87%)</td>
<td>342</td>
<td>159</td>
<td>93</td>
</tr>
<tr>
<td>Scorpion anti-venom</td>
<td>388 (57%)</td>
<td>225</td>
<td>94</td>
<td>69</td>
</tr>
<tr>
<td>Deaths</td>
<td>61 (9.8%)</td>
<td>41</td>
<td>12</td>
<td>8</td>
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<tr>
<td>Hospital stay (days)</td>
<td>2.9 ± 3.1</td>
<td>2.6 ± 2.4</td>
<td>2.97 ± 3.2</td>
<td>3.8 ± 4.9</td>
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</table>

Group 1: age ≤ 5 years; group 2: age = 6–10 years; group 3: age > 10 years. LC = lung crackles; SBP = systolic blood pressure; DBP = diastolic blood pressure; MV = mechanical ventilation.
associated with poor outcome (Table 5). Additionally, there was a strong association between the number of organ failures and outcome (Figure 5). As shown in Table 6, the presence of SIRS was significantly associated with pulmonary edema, cardiac failure, respiratory failure, agitation, coma, and grade III envenomation. Moreover, a temperature >39°C was significantly associated with pulmonary edema (P < 0.0001), heart failure (P < 0.0001), cardiogenic shock (P < 0.01), and neurological failure (P < 0.05). Additionally, a body temperature >39°C was associated with the diagnosis of pulmonary edema, with a sensitivity of 20.6%, a specificity of 94.4%, and a positive predictive value of 97.7%. In our study, a white blood cell count >25,000 cells/mm³ was associated with neurological failure (P < 0.05). Although there was no significantly association between a white blood cell count >25,000 cells/mm³ and the presence of pulmonary edema (P > 0.05), we found that most patients (84.3%) with a white blood cell count >25,000 cells/mm³ developed pulmonary edema. (Figure 6). Finally, a significant association was found between blood glucose levels above 15 mmol/L and the presence of the pulmonary edema (P = 0.005), we found that most patients (84.3%) with a white blood cell count >25,000 cells/mm³ developed pulmonary edema. (Figure 6). Finally, a significant association was found between blood glucose levels above 15 mmol/L and the presence of pulmonary edema, with a sensitivity of 27.5%, a specificity of 87.4%, a positive predictive value of 88.2%, and a negative predictive value at 26% (Figure 7).

### Table 3

<table>
<thead>
<tr>
<th>Number of organ failures</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>133</td>
<td>19.42</td>
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<tr>
<td>1</td>
<td>109</td>
<td>15.92</td>
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<tr>
<td>2</td>
<td>378</td>
<td>55.18</td>
</tr>
<tr>
<td>3</td>
<td>58</td>
<td>8.46</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>0.88</td>
</tr>
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<td>5</td>
<td>1</td>
<td>0.14</td>
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### Table 4

<table>
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<th>Parameters</th>
<th>Deaths (61)</th>
<th>Survivors (624)</th>
<th>P</th>
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<tr>
<td>Age (years)</td>
<td>5.4 ± 4</td>
<td>6 ± 4</td>
<td>0.27</td>
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<tr>
<td>Sex (male/female)</td>
<td>32/29</td>
<td>399/286</td>
<td>0.33</td>
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<tr>
<td>Mean time between sting and admission (&lt;2 hours)</td>
<td>3</td>
<td>49</td>
<td>0.01</td>
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<tr>
<td>HR</td>
<td>139 ± 21</td>
<td>134 ± 21</td>
<td>0.07</td>
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<tr>
<td>SBP (mmHg)</td>
<td>72 ± 24</td>
<td>89 ± 20</td>
<td>&lt; 0.001</td>
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<tr>
<td>Agitation (yes/no)</td>
<td>53/8</td>
<td>505/119</td>
<td>&lt; 0.05</td>
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<tr>
<td>Sweating (yes/no)</td>
<td>47/14</td>
<td>490/134</td>
<td>&lt; 0.05</td>
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<tr>
<td>Fever (%)</td>
<td>81%</td>
<td>50%</td>
<td>0.01</td>
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<tr>
<td>Cardiogenic shocks</td>
<td>60%</td>
<td>22%</td>
<td>&lt; 0.001</td>
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<td>Pulmonary edema (yes/no)</td>
<td>60/1</td>
<td>374/250</td>
<td>&lt; 0.001</td>
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<tr>
<td>Coma (yes/no)</td>
<td>18/43</td>
<td>105/519</td>
<td>0.01</td>
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<tr>
<td>Bilateral mydriasis (yes/no)</td>
<td>5/56</td>
<td>9/615</td>
<td>&lt; 0.001</td>
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<td>Diarrhea (yes/no)</td>
<td>7/54</td>
<td>29/595</td>
<td>0.023</td>
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<td>Blood glucose levels (mmol/L)</td>
<td>14.7 ± 7.2</td>
<td>11.3 ± 5.7</td>
<td>&lt; 0.001</td>
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<td>Use of inotrope (yes/no)</td>
<td>61/0</td>
<td>453/171</td>
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<td>Mechanical ventilation</td>
<td>59/2</td>
<td>210/214</td>
<td>&lt; 0.001</td>
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<td>(yes/no)</td>
<td>53/8</td>
<td>541/83</td>
<td>&gt; 0.05</td>
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<tr>
<td>Use of steroids (yes/no)</td>
<td>94%</td>
<td>61%</td>
<td>&lt; 0.001</td>
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<td>Scorpion anti-venom (%)</td>
<td>42.7 ± 10.7</td>
<td>19.3 ± 10.7</td>
<td>&lt; 0.001</td>
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<td>PRISM</td>
<td>379</td>
<td>120</td>
<td>&lt; 0.001</td>
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<tr>
<td>Hospital stay (days)</td>
<td>4.36 ± 6.5</td>
<td>2.8 ± 2.6</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**HR** = heart rate.

### Table 5

<table>
<thead>
<tr>
<th>Type of organ failure</th>
<th>Number</th>
<th>Deaths</th>
<th>Survivors</th>
<th>P</th>
</tr>
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<tr>
<td>Heart failure</td>
<td>Yes</td>
<td>542</td>
<td>11%</td>
<td>89%</td>
</tr>
<tr>
<td>No</td>
<td>143</td>
<td>0%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>Yes</td>
<td>444</td>
<td>13.5%</td>
<td>86.5%</td>
</tr>
<tr>
<td>No</td>
<td>241</td>
<td>0.4%</td>
<td>99.6%</td>
<td></td>
</tr>
<tr>
<td>Neurological failure</td>
<td>Yes</td>
<td>25</td>
<td>40%</td>
<td>60%</td>
</tr>
<tr>
<td>No</td>
<td>660</td>
<td>7.7%</td>
<td>92.3%</td>
<td></td>
</tr>
<tr>
<td>Kidney failure</td>
<td>Yes</td>
<td>13</td>
<td>38.5%</td>
<td>61.5%</td>
</tr>
<tr>
<td>No</td>
<td>672</td>
<td>8.3%</td>
<td>91.7%</td>
<td></td>
</tr>
<tr>
<td>Liver failure</td>
<td>Yes</td>
<td>7</td>
<td>57%</td>
<td>43%</td>
</tr>
<tr>
<td>No</td>
<td>678</td>
<td>8.4%</td>
<td>91.6%</td>
<td></td>
</tr>
<tr>
<td>Haematological failure</td>
<td>Yes</td>
<td>7</td>
<td>14.3%</td>
<td>85.7%</td>
</tr>
<tr>
<td>No</td>
<td>678</td>
<td>8.8%</td>
<td>91.2%</td>
<td></td>
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**DISCUSSION**

Our study confirms the correlation between young age and severity of clinical manifestations after scorpion envenomation. In fact, in our study, the mean PRISM score on admission was at 21.5 ± 12.6 points; it was above 30 in 29.5%, showing the severity of envenomation in our patients. Moreover, SIRS was observed in 555 patients (81%), and 552 patients (80.6%) developed failure in one or more organ systems. Scorpion envenomation is common in tropical and subtropical regions. The venom distribution in the extravascular compartment is fast, explaining the early appearance of the symptoms. The evolution of the symptoms is rapid. Three stages of increasing severity can be distinguished. Stage I corresponds to benign envenomations. Pain is immediate, intense, and persistent, with feelings of partial recoveries and relapses. The passage to the following stages is generally unforeseeable and rapid. The critical period range is between the third and twelfth hour, during which the risk of a complication is the highest. Stage II corresponds to severe envenomation with systemic manifestations. Entry in the next stage, often brutal, occurs between the fourth and the twelfth hour after the sting in 5–10% of stage II cases. Stage III corresponds to a very severe envenomation, potentially lethal. At this stage, the risk of cardiovascular collapse is the highest, associated with major respiratory complications: pulmonary edema, bronchospasm, and cyanosis. At this stage, the evolution can be fatal in a few hours, sometimes in a few minutes, involving about one-half of the cases. Most of these complications and deaths are preventable. The main preventable
factors include inability to early recognize the severity and delay in referring victims to specific health-care facilities. Hospital-related preventable factors in endemic areas include inadequate skills and lack of ICUs. Indeed, delay in seeking emergent treatment contributes to most of rural deaths. Although there seems to have been a slight drop in scorpion envenomation mortality, the number of needless death remains high. Failure to early identify high-risk patients at the first-line health care was considered as one of the potential causes of this failure. Although there is no consensus on the criteria for hospital admission, several recommendations suggest that all patients should be observed up to 4 hours in the first-line care facility before transfer to the nearest community-based hospital. However, for high-risk patients (young children), this observation period will be a waste of time and could adversely affect outcome, because their transfer from rural setting to the nearest hospital will likely be unsafe and too late. In fact, in young children, envenomation can evolve directly from stage I to III. For these reasons, evaluation of the severity of the envenomation, mainly in children, is essential to establish the prognosis and institute adequate treatments. In our study, pulmonary edema, coma, use of catecholamine, and death are less frequently observed in the subgroup with shorter interval (<2 hours) from the time of the sting until medical consultation. Moreover, we found, in the present study, that there is a decrease of scorpion stings over the time. However, our study includes only severe sting patients requiring admission in the ICU (grade II included patients with systemic manifestations, and grade III included patients with cardiorespiratory manifestations and/or severe neurological manifestations). The decrease of the number of severe scorpion-sting patients requiring ICU admission can be explained by the fact that Tunisian heath authorities began to recognize the importance of the problem and the need for emergent intervention. They understood that the primary health-care system at the district and subdistrict levels needed strengthening to provide adequate medical services. During the past few years, projects were designed to upgrade some district hospitals, and several ICUs were created. As a consequence, currently, severe forms of scorpion envenomation are now admitted and treated in ICUs of rural hospitals.

Factors that can affect the severity of scorpion envenomation are health status of the victim as well as the age and weight. Children are more susceptible to scorpion envenomations, and the clinical manifestations of envenomation may be more severe in children and result in multi-organ failure and death. The clinical manifestations of scorpion envenomation seem to be secondary to activation of both the sympathetic and parasympathetic nervous systems. Although the venoms of certain species may produce apnea, bradycardia, and hypotension, activation of the sympathetic nervous system more commonly leads to hypertension and pulmonary edema. Severe scorpion envenomations, characterized by cardiovascular, pulmonary, and neurological manifestations,

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SIRS (+)</th>
<th>SIRS (−)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Pulmonary edema</td>
<td>Yes</td>
<td>374 (86%)</td>
<td>60 (14%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>90 (63%)</td>
<td>52 (37%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Yes</td>
<td>463 (85%)</td>
<td>79 (15%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>92 (64%)</td>
<td>51 (36%)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>Yes</td>
<td>384 (86.5%)</td>
<td>60 (13.5%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>171 (71%)</td>
<td>70 (29%)</td>
</tr>
<tr>
<td>Agitation</td>
<td>Yes</td>
<td>464 (83%)</td>
<td>94 (17%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>91 (71%)</td>
<td>36 (29%)</td>
</tr>
<tr>
<td>Coma</td>
<td>Yes</td>
<td>91 (88%)</td>
<td>13 (12%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>373 (79%)</td>
<td>99 (21%)</td>
</tr>
<tr>
<td>Stage</td>
<td>II</td>
<td>125 (72%)</td>
<td>49 (28%)</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>430 (84%)</td>
<td>81 (16%)</td>
</tr>
</tbody>
</table>

Figure 6. Association between leukocytes counts and the presence of pulmonary edema.

Figure 7. Association between blood sugar and the presence of pulmonary edema.
can be life-threatening as a result of complications such as myocardial dysfunction, shock, pulmonary edema, or hypertensive encephalopathy. Scorpion toxins also may produce severe central nervous system manifestations, including marked irritability and unconsciousness.\(^8,18\)

This correlation between age and severity can be explained by the fact that, for the same quantity of venom inoculated, the serum levels of venom will be higher in children than in adult patients.\(^8\) Moreover, it is possible that in children, there is higher uptake in the heart and other organs.\(^8\) Although symptoms and clinical signs of scorpion envenoming are traditionally explained as the result of the massive release of catecholamines\(^39\) or a direct effect of scorpion venom,\(^21,22\) several studies have emphasized the relevance of pro-inflammatory mediators in the pathophysiological manifestations of human scorpion envenomation.\(^23–26\) Cytokines are produced by immune and non-immune cells when challenged by various environmental or inflammatory insults and mediate almost all phases of the inflammatory process.\(^7,24,25,27–29\) In our study, the levels of inflammatory markers (cytokines) were not tested. However, clinical indicators predictive of inflammatory response were observed in most patients (81%), and 552 patients (80.6%) developed failure in one or more organs. Moreover, the presence of SIRS and/or a temperature > 39°C was significantly associated with pulmonary edema, cardiac failure, respiratory failure, agitation, coma, and grade III envenomation.

The severity of envenomation is related to neurological and cardio-respiratory dysfunction.\(^30–37\)

In the current study, 434 (63.4%) patients had pulmonary edema. Moreover, pulmonary edema and cardiogenic shock were associated with poor outcome. The mechanism of scorpion envenomation-induced cardiac dysfunction is still unclear.\(^38\) Gueron and others\(^39\) hypothesized that catecholamine storm post-envenomation may cause cardiac dysfunction by catecholamine-induced hypoxia and that death might result from myocarditis and congestive heart failure.\(^40\) Some authors suggested that cardiac dysfunction in scorpion envenomation may be because of a direct effect of scorpion venom.\(^21,22,41,42\) More recently, we suggested\(^11\) that the seriousness of scorpion envenomation resulting essentially from cardiac dysfunction is not only because of the release of catecholamine but also the effect of the cytokines and/or neuropeptide Y on the coronary vessels, leading to myocardial ischemia.\(^7,24\) In our study, a high value of blood glucose level was associated with a poor outcome \((P < 0.001)\). Moreover, a significance between blood glucose levels above 15 mmol/L and the presence of pulmonary edema \((P = 0.001)\) and heart failure \((P = 0.003)\) was found. In fact, blood glucose levels above 15 mmol/L were associated with the diagnosis of pulmonary edema, with a specificity of 87.4% and a positive predictive value of 88.2%. This association between hyperglycemia and left ventricular dysfunction can be explained by several factors.\(^45–48\) Although leukocytosis is often described after scorpion envenomation, its correlation with the pulmonary edema after scorpion envenomation has been rarely described in the literature.\(^38\) In our study, leukocytosis of more than 25,000 cells/mm\(^3\) was not associated with pulmonary edema. We found that most patients (84.3%) with leukocytes levels > 25,000 cells/mm\(^3\) developed pulmonary edema. Treatment of scorpion envenomation has two components: anti-venom treatment and supportive care. Anti-venom must be administered as early as possible and through the venous route.\(^1\) The anti-venom dose depend on the severity of symptoms and the amount of inoculated venom. When the latter is about 30–50 DL\(_{50}\) of neutralized venom per milliliter of anti-venom, the treatment requires from 5 mL, in mild envenomations, to 20 mL or more, in the case of severe envenomations. Most of the anti-venoms currently manufactured are purified fragments of immunoglobulins F(ab')\(_2\), which reduce adverse effects.\(^3\) However, the anti-venom neutralizing titer is essential of anti-venom efficacy.\(^47\) A low neutralizing titer may be compensated for by the administration of higher doses, increasing the risk of adverse reactions, such as shock or anaphylaxis, which necessitate a rapid treatment with adrenaline. However, the effectiveness of anti-venom is controversial in scorpion-sting treatment. In Mexico\(^48\) and Brazil,\(^49\) there is overwhelming statistical evidence of its effectiveness in reducing pediatric scorpion-sting mortality, but in Israel\(^50\) and India,\(^51\) there are intensivists who strongly advocate against anti-venom. In a more recent study among critically ill children with neurotoxic effects of scorpion envenomation, Boyer and others\(^52\) found that intravenous administration of scorpion-specific F(ab')\(_2\) anti-venom resolved the clinical syndrome within 4 hours, reduced the need for concomitant sedation with midazolam, and reduced the levels of circulating unbound venom. In Tunisia, scorpion anti-venom was usually given in severe scorpion envenomation (grade II and grade III) as an intravenous infusion of bivalent scorpion anti-venom (batch number 85) corresponding to 95% or more F(ab')\(_2\).\(^53\) According to the manufacturer (Institut Pasteur, Tunis, Tunisia), 1 mL of anti-venom administered to Swiss mice (weight = 18–22 g) neutralizes 10 LD\(_{50}\) (the dose required to kill 50% of animals) of the venom of A. australis and B. occitanus.\(^53\) This specific anti-venom used was not changed over time. In a prospective, randomized, and controlled trial to assess the efficacy of routine administration of scorpion anti-venom to scorpion-stung patients, irrespective of clinical severity, Abroug and others\(^53\) found no evidence of beneficial effects of routine administration of scorpion anti-venom to stung patients, irrespective of clinical severity. Curative and preventive effects, rate of hospital admission, mortality, or need of mechanical ventilation were similar in the scorpion anti-venom and placebo groups.

In our study, 388 patients (56.6%) received scorpion anti-venom before arriving in the ICU. The use of scorpion anti-venom was associated with poor outcome in univariate analysis; however, multivariate analysis indicated that anti-venom did not affect outcome. However, we cannot obtain any conclusion. In fact, this is a retrospective study during a period of 13 years, and the dose, interval between sting and administration, route of administration of scorpion anti-venom, and cause of not administrating scorpion anti-venom in the scorpion anti-venom-free group were not available in most medical records. Moreover, specific changes in symptom intensity and development of serum sickness were not available in medical records.

In summary, this analysis showed that intoxications caused by scorpions in the south Tunisia region were mostly seen in hot summer months, especially in July and August. The majority of the cases were in the age group less than 5 years. In clinical evaluations, both local and systemic effects were observed. We think that, in many of these cases, the children were stung because of careless behavior such as walking barefoot, lifting up stones, and putting on clothes and shoes without checking...
SCORPION ENVENOMATION AMONG CHILDREN

them for the presence of scorpions. We postulate that prevention is highly warranted. This prevention is based first on the use of protective clothing, such as shoes, that may prevent some scorpion envenomations. Second, shoes, clothing, and backpacks should be checked for scorpions before use. Third, yards should be kept free of debris, which can serve as a place for scorpions to hide. Fourth, windows and doors should fit tightly to prevent scorpions from entering the house. Moreover, avoid walking barefoot, especially at night, when scorpions are active. Finally, each envenomed patient should be admitted into an ICU setting because of the unpredictability of the symptoms, the risks associated with anti-venom administration, and the need for airway or blood-pressure support.

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REFERENCES


