

## Acute kidney injury and pancreatitis due to scorpion sting: case report and literature review

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### ABSTRACT

Despite the high number of accidents due to scorpion stings in Brazil, severe cases in adults are seldomly reported. In the Northeast region of Brazil, *Tityus stigmurus* is the most prevalent species. A 69 year-old woman who was stung by a scorpion attended the emergency room 5 hours after envenomation. She got worse due to abdominal pain. Clinical findings were concordant with class III scorpion envenomation (major systemic manifestations), complicated by acute kidney injury and acute pancreatitis. Intensive supportive therapy was adopted. In the follow-up, 3 months later, she was completely recovered. This report is being brought to recommend the thorough management of victims of scorpion accidents, enabling early diagnosis of severe complications, which could lead to death if aggressive supportive measures are not early and adequately taken.

**KEYWORDS:** Scorpionism. Acute kidney injury. *Tityus stigmurus*. Acute pancreatitis.

### INTRODUCTION

Scorpion envenomation is reported in many parts of the world and is more frequent in tropical and subtropical countries<sup>1,2</sup>. It is an important public health problem in Brazil due to its high frequency and potential to cause severe clinical manifestations, which could even be fatal<sup>3,4</sup>. It is estimated that almost 2.5 million people in the world live in areas at risk for scorpion stings and more than 1.5 million of envenomations occur each year, causing around 2,600 deaths<sup>5</sup>. However, according to World Health Organization (2007), the real number of scorpion's stings in the world are underestimated<sup>6</sup> and literature data are insufficient<sup>5</sup>.

Since the early 2000s, the number of scorpion envenoming cases in Brazil have increased. In the State of Ceara, Northeast of Brazil, from 2007 to 2016, 28,402 accidents due to venomous animals were registered, from which 65.1% were caused by scorpion stings, followed by snakebites (23.4%)<sup>7</sup>.

Scorpion sting is a relevant cause of human envenomation, which is included in the group of neglected tropical diseases in developing countries<sup>8</sup>. Although 1,500 scorpion species have been described, about 30 species are considered dangerous to humans. In Brazil, the majority of scorpion envenomations are caused by four species: *Tityus stigmurus*, *T. bahiensis*, *T. paraensis* and *T. serrulatus*. Most scorpion sting victims present a benign course, but complications can occur, and severe envenoming is usually due to *T. serrulatus*<sup>8-10</sup>.

The diagnosis of scorpion sting is based on epidemiological features, clinical signs, symptoms, and exclusion of other etiologies. The clinical presentation

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of envenomation is relatively similar, regardless of the species, and includes neurotoxic syndromes mediated by sympathetic and parasympathetic systems<sup>3,11</sup>. Nevertheless, differences between species may depend on associated factors to each species and to each patient, such as age, part of the body stung, body mass, immune status, sensitivity to venom and time elapsed after sting<sup>12</sup>.

Most scorpion envenomations only cause immediate local pain, however it can be accompanied by swelling, hyperemia, paresthesia and piloerection. The development of systemic syndromes presumes a potential severity that can turn into a life-threatening emergency episode<sup>1,13</sup>, with cardiovascular complications (myocardial infarction, heart failure, shock, arrhythmia, or severe hypertension); pulmonary (including pulmonary edema); gastrointestinal (acute pancreatitis, peptic ulcer, bleeding); metabolic (hyperglycemia, hypocalcemia, hyperkalemia); and neurological complications (hypertensive encephalopathy, stupor, coma, convulsions)<sup>11</sup>.

According to Khattabi *et al.*<sup>14</sup>, there are three classifications for scorpion stings, which had been proposed by experts from many countries. This classification was based exclusively on signs and symptoms, not taking into account the risk factors, vulnerable groups for severity, animal species or time between the accident and medical assistance. Class I includes only local manifestations (burning sensation, necrosis, paresthesia, pain, petechiae). Class II includes minor manifestations, which are not life-threatening (abdominal distension, hypertension, thirst, hyperthermia, urinary retention, hypothermia, vomiting, wheezing, hematuria, pancreatitis), although there was not total consensus for all signs and symptoms. Class III represents systemic injuries, severe manifestations, which offer threatening to life, such as cardiogenic, respiratory and neurologic failure.

There are few cases of kidney injury due to scorpion stings reported in the literature. The direct effect of scorpion venom on the kidneys and damage resulting from intravascular hemolysis disseminated intravascular coagulation (DIC), hemolytic uremic syndrome and hypovolemia have been investigated in clinical and experimental studies<sup>15</sup>. The early detection of the occurrence of acute kidney injury (AKI) is essential in these patients because the consequences can be very severe if not correctly managed.

Acute pancreatitis is another unusual manifestation after scorpion sting and has been described in human victims stung by the genre *Tityus* and *Leiurus*<sup>16</sup>. Pancreatitis diagnosis is based on clinical manifestations and laboratory tests such as elevated serum amylase and lipase. Moreover, abdominal pain, nausea, vomiting are common signs

and symptoms reported in acute pancreatitis secondary to scorpion sting<sup>17</sup>.

The aim of this study is to describe a rare case of a scorpion sting complicated by AKI and acute pancreatitis in an elderly patient successfully treated in a reference toxicological assistance center in Brazil, highlighting the main findings of the available studies in medical literature, providing brief guideline on its clinical management.

## CASE REPORT

A 69 year-old woman, with previous systemic arterial hypertension (SAH) and diabetes mellitus (DM), was stung in the right hand by a scorpion, which had been brought by the patient and been identified as a *Tityus stigmurus*, the most prevalent in Brazilian Northeastern. The animal was about 5 centimeters in length, with yellowish-brown color and a black line on the back. Toxicologists did not report the animal sex, but this species is parthenogenetic and the majority of these scorpions are female. This scorpion feeds mainly on cockroaches, which are abundant in residences from urban or rural areas. The accidents commonly happen inside the house, similarly to this reported case.

The time elapsed until emergency admission was about five hours after the sting and she reported severe abdominal pain, one episode of emesis and sweating. Seven hours after the sting, she presented worsening of symptoms and received vigorous venous hydration and primary medical care.

Upon admission, the patient presented a compromised general condition, lowered consciousness level (Glasgow Coma Scale Score of 11, in a scale from 3-15) and blood pressure was 150 x 110 mmHg. The clinical abdominal exam revealed pain on superficial palpation. Body temperature was normal (36 °C). Cardiac auscultation was normal.

The arterial blood gas analysis (Table 1), performed in the emergency room, revealed increased lactate levels. The first electrocardiogram showed sinus rhythm, with left atrial hypertrophy and a possible old anteroseptal infarct. The second electrocardiogram presented sinus rhythm with signs of hypokalemia. An urgency ultrasonography was performed revealing moderate hepatic steatosis and normal-sized kidneys. The results of initial laboratory tests including creatinine, urea, chloride, creatine phosphokinase, coagulogram and sodium were all in the normal range (Table 1). The values of glucose, liver enzymes (sAST and sALT), lipases, amylases, leukocyte count and D-lactate dehydrogenase (D-LDH) were increased. Additionally, the serum potassium value was decreased (below the normal range).

As soon as possible, intensive care measures were established based on the continuous monitoring of

**Table 1** - Laboratory findings on admission and during the follow-up of the patient after the scorpion sting

Variable	Admission	24 hours later	Discharge	3 months later	Normal range
Glucose (mg/dl)	281	235	**	**	74 - 106
Potassium (mmol/l)	3.24	3.92	3.06	4.13	3.5 - 5.3
Sodium (mmol/l)	140	141	133	142	135 - 148
Chloride (mmol/l)	100	106	93	96	96 - 109
Urea (mg/dl)	27	45	50	42	13 - 43
Creatinine (mg/dl)	0.8	1.4	1.0	0.8	0.6 - 1.1
AST (U/L)	85	240	**	20	< 32
ALT (U/L)	93	242	**	19	< 31
PT (s)	12.1	14.2	11.8	11.4	10 - 14
aPTT (s)	22.2	26.5	24.8	23.9	22 - 28
Lipase (U/L)	5442	2121	**	70	13 - 60
Amylase (U/L)	1914	1138	135	92	< 84
D-LDH (U/L)	474	**	**	319	230 - 460
CK (U/L)	91	**	**	102	< 170
Hemoglobin (g/dl)	14.2	15.6	9.9	13.6	11.3 - 15.2
Leukocytes (/mm <sup>3</sup> )	11470	7730	10110	5170	3600 - 10000
Platelets (/mm <sup>3</sup> )	164000	162000	218000	202000	150 - 450 (10 <sup>3</sup> )
Creatinine (mg/dl)	0.8	2.4	1.0	0.8	0.6 - 1.1
Urea (mg/dl)	27	115	50	42	13 - 43
MCP-1 (pg/mgCr)	1576.97	**	**	**	*
uNGAL (ng/mgCr)	7.97	**	**	**	*
KIM-1 (ng/mgCr)	1180	**	**	**	*
PH***	7.41	**	**	**	7.35
pCO <sub>2</sub> (mmHg)***	37.1	**	**	**	35 - 45
pO <sub>2</sub> (mmHg)***	161.3	**	**	**	85 - 100
HCO <sub>3</sub> (mmol/L)***	23.6	**	**	**	22 - 26
BE (mmol/L)***	-1.6	**	**	**	-4 - +4
Lactate (mmol/L)***	2.54	**	**	**	<2.0

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; D-LDH: D-lactate dehydrogenase; CK: Creatine phosphokinase; PT: Prothrombin time; aPTT: partial time of thromboplastin; uNGAL: Urinary Neutrophil Gelatinase-Associated Lipocalin; KIM-1: Kidney Injury Molecule-1; MCP-1: Monocyte Chemoattractant Protein-1. \*Ranges in Institutional Control Group (normalised to urinary creatinine) - MCP-1: 0-124.5pg/mgCr; uNGAL: 0.57-21.09ng/mgCr; KIM-1: 399.88-1162.09ng/mgCr. \*\* Not available. \*\*\*Arterial Gasometry

cardiac and respiratory function. Firstly, a rigorous water balance was performed and the patient received scopolamine bromide and tramadol intravenously resulting in efficient analgesia. She received promethazine (50 mg intramuscular) as a pre-antivenom treatment. Scorpion antivenom was administered (six vials intravenously), without anaphylactic symptoms. Prolonged fasting was prescribed for treatment of acute pancreatitis and insulin administration for glycemic control. Furthermore, she received potassium chloride (vials at 10%) in order to stabilize serum levels.

During hospital stay, the patient presented a hypertensive peak that reached 188 x 140 mmHg and she received captopril (25 mg), hydrochlorothiazide (25 mg) and amlodipine (10 mg), with adequate blood pressure control. After the antivenom administration, the patient reported improvement of abdominal pain, while amylase and lipase returned to normal levels in a few days.

Despite the abdominal symptoms improvement, the patient developed non-oliguric AKI, according the KDIGO criteria<sup>18</sup>, two days after admission. The nephrologist's opinion was requested and a conservative treatment with

increase intravenous hydration was prescribed, and an improvement of the renal function was promptly observed (Table 1). The patient progressed with clinical and laboratory improvement. After 11 days, the patient was completely stable and was discharged for an outpatient follow-up. She received a prescription of captopril (25 mg), hydrochlorothiazide (25 mg) and subcutaneous insulin (NPH, 10 UI in the morning).

Three months later, the patient returned with total recovery of renal and pancreatic functions, asymptomatic, with normal blood pressure (120 x 60 mmHg). The medicines for hypertension and diabetes were maintained.

## DISCUSSION

Scorpion envenomation is still a relevant environmental health issue in tropical and subtropical regions, such as Brazil. Severe cases are notified every year and deaths involving children were caused by *Tityus* genus<sup>19-21</sup>. The reported case highlighted rare complications in the same patient, AKI and acute pancreatitis, both potential fatal conditions, which were overcome with early and adequate intensive treatment.

In urban areas of the Northeast of Brazil, *T. stigmurus* is the most important health-threatening scorpion species<sup>20</sup>. Most reported cases occur in children younger than 15 years old and they frequently represent severe envenomation<sup>20</sup>. In Brazil, epidemiological data are incomplete and controversial, so there is scarcity of clinical information about scorpion envenomation in adults, probably due to the reduced severity of cases.

Scorpion venoms are rich sources of small peptide toxins and the most important toxins with medical consequences are  $\alpha$ -toxins, which consist of 61-76 polypeptides that bind to a specific site on the mammalian voltage-gated sodium channel. Once the toxins bind to a site, inhibition of the inactivation of that channel begins, resulting in prolonged depolarization and, hence, neuronal excitation<sup>22</sup>. Scorpion toxins have been studied worldwide and, recently, a new family of peptides of *Tityus stigmurus* called Hypotensins (TSTI0006C)<sup>23</sup> was discovered, showing a molecular mass of 2.7 kDa, absence of cysteines and presence of two C-terminal proline residues, which are bradykinin-potentiating peptide signature. This hypotensin identified in *T. stigmurus* scorpion venom was able to potentiate the action of bradykinin inducing relaxation in mesenteric artery rings, independent of angiotensin converting enzymes, without cytotoxicity<sup>23</sup>.

The patient reported here was an old female presenting compromised general condition and abdominal pain secondary to scorpion sting, consistent with Class III

scorpion envenomation (major systemic manifestations) within a period of 5 hours after the sting. She was then transferred to an intensive care unit for monitoring, not only due to her clinical condition, but also due to her comorbidities (diabetes mellitus, systemic arterial hypertension and advanced age). Although it is not common to find severe scorpion envenomations in adults, physicians should consider the risk of clinical complications if the patient has multiple comorbidities. Otherwise, there are few studies focusing on elderly people regarding envenomations. Management of elderly people is always a challenge, in terms of associated clinical comorbidities and the greater medical, social and financial resources involved, inasmuch these patients are more prone to hemodynamically instability and are more vulnerable<sup>24</sup>. Interestingly, a study performed in patients over 65 years, victims of snakebite in the United States highlighted the existence of comorbidities and the use of a variety of medications, which may increase their risk of hemotoxicity, although the risk of bleeding and other complications was not increased in this group<sup>25</sup>.

Scorpion envenomations are ubiquitous. However, severe manifestations are rare. The venom has very low levels of enzyme activity compared to that of snakes or hymenoptera venom. However, in the present case, the patient presented local clinical manifestations as pain and edema, and systemic manifestations, such as somnolence, hypertension, abdominal pain and previous episodes of emesis. In human envenomations caused by the *Tityus* genus, neurological manifestations such as convulsion and lowering of the consciousness level have been described<sup>20,21,26</sup>. Other rare clinical conditions have been described due to scorpions, as ischemic stroke<sup>27</sup>, acute kidney injury<sup>28</sup>, myocardial dysfunction<sup>29</sup> and death.

Although scorpion venom causes an inflammatory reaction largely mediated by cytokines in the lungs, kidneys, heart and intestine of experimental rats<sup>30</sup>, acute pancreatitis is an unusual clinical manifestation caused by scorpion envenomation<sup>29,31</sup>. Bartholomew *et al.*<sup>32</sup> conducted an experimental study in dogs in order to clarify the etiology of acute scorpion pancreatitis in dogs that received venom of *Tityus trinitatis*. In this experiment, scorpion venom stimulated pancreatic exocrine secretion, associated with a serial rise in serum amylase. Otherwise, the autopsy findings of dogs demonstrated edema of duodenal papilla and duodenitis. In another study, effects were observed in the organs during various stages of scorpion envenomation due to *T. trinitatis*, such as salivation, lacrimation and cardiac arrhythmias. The authors suggested that the secretory action of the scorpion could also be caused by the release of acetylcholine from nerve endings to the pancreas<sup>33</sup>. Chen *et al.*<sup>34</sup> conducted a study with Australian

possums to characterize the effects of *Tityus serrulatus* venom on the biliary gall bladder, Oddi's sphincter, duodenal motility and the pancreatic exocrine secretion. They demonstrated that intravenous or close intra-arterial infusion of scorpion venom resulted in transient profound responses in biliary and duodenal motility. These effects occurred early following infusion and could explain the upper gastrointestinal symptoms which accompany scorpion envenomation<sup>34</sup>.

There are very few cases reported about pancreatic involvement due to scorpion envenomation<sup>13,17,35-38</sup>, as summarized in Table 2. According to this review, the prevalence of acute pancreatitis due to scorpion in children is noteworthy, and in children abdominal pain and high levels of amylases can be absent upon admission. In the study of Bartholomew *et al.*<sup>35</sup>, which was described over a two-month period, 30 patients were admitted to hospital following scorpion stings of the *Tityus* genus in Trinidad. In this study, 24 cases of acute pancreatitis occurred right after the scorpion sting. In about 80% of cases

hyperamylasemia was present<sup>35</sup>. The clinical presentation of our patient led the physician to investigate the cause of abdominal pain. Additionally, the increasing levels of amylases and lipases, allowed the diagnosis of acute pancreatitis, which was fundamental for the improvement of the patient's management after fasting. It is possible that some cases of mild acute pancreatitis due to scorpionism were not identified because patients did not refer abdominal symptoms.

The mainstay of pancreatitis pathogenesis due to scorpion sting is the cholinergic discharge induced by its toxins<sup>13,35-37</sup>. Bartholomew *et al.*<sup>35</sup> discussed about the multiple mechanisms of acute pancreatitis. The authors reported obstruction of the common bile duct, a powerful effect on the autonomic nervous system, similarly to the salivation (purely neurogenic action), an appreciable amount of serotonin, which could lead to the increment of capillary permeability and free trypsin releasing kallikrein, which is a precursor of the hypotensive bradykinin. The toxin-mediated cholinergic discharge that takes place in

**Table 2** - Case reports of pancreatic involvement due to scorpion sting

References	Number of cases	Age <sup>a</sup>	Scorpion Specie	Initial presentation <sup>e</sup>	Antivenom	Complications <sup>f</sup>	Outcome	Pancreatic findings <sup>g</sup>
Bartholomew <i>et al.</i> , 1970 <sup>35</sup> , Trinidad	30 (20 males)	9 – 57 <sup>c</sup>	<i>Tityus trinitatis</i>	Sialorrhea (16), abdominal pain (16), vomit (15), reddening and oedema in stung site	No	No	Discharge without symptoms	High amylase level (24), high transaminases levels (5)
Sofer <i>et al.</i> , 1991 <sup>17</sup> , Israel	15 (9 males)	1 – 14	<i>Leiurus quinquestriatus</i> and <i>Buthotus judaicus</i>	Abdominal pain (3), vomit (7), hematemesis (1), respiratory failure (1), hypertension (6), ventricular arrhythmias (1)	No	Respiratory failure (assisted ventilation) and Cardiac abnormalities	1 death (ventricular arrhythmia)	High level of serum immunoreactive cationic trypsin (13), hyperglycaemia
Otero <i>et al.</i> , 2004 <sup>36</sup> , Colombia	1 (female)	3	<i>Tityus asthenes</i>	Vomit, tachypnoea	b	b	Discharge without symptoms	Acute oedematous pancreatitis
Sousa <i>et al.</i> , 2007 <sup>37</sup> , Venezuela	2 (2 males)	8; 13	<i>Tityus neoespartanus</i>	Local pain in right foot (2), vomit (2), colic-like abdominal pain (2), sialorrhea (2), diaphoresis (2)	03 vials in the 13 year-old-patient	Cardiac abnormalities and pancreatic microcalcifications (abdominal ultrasound, 1 year later)	Discharge without symptoms	High levels of amylase and lipase, edematous pancreatic pattern (abdominal ultrasound)
Mouaffak <i>et al.</i> , 2012 <sup>38</sup> , Africa	1	11	<i>Androctonus mauretanicus</i>	Abdominal pain, tachycardia, tachypnoea, agitation, fever	b	Priapism	Discharge without symptoms	Normal abdominal ultrasound
Kumar <i>et al.</i> , 2012 <sup>13</sup> , India	1 (male)	8	b	Autonomic dysfunctions, pulmonary oedema, stung site – right foot without abnormalities	b	Haemorrhagic pancreatitis, myocarditis and pulmonary oedema	Death	Extensive parenchymal pancreatic necrosis accompanied by interstitial haemorrhagic pancreatitis ( <i>post-mortem</i> diagnosis)

a Years old; b Not reported; c Minimum – maximum; d Increase in serum creatinine or decrease in its clearance by more than 50% of standard values was considered as renal failure; e- number of patients with described characteristic were represented between parenthesis; f- haemorrhagic pancreatitis, pseudocyst formations.

the pancreas might promote premature activation of the enzymes produced within the acinar cell. These enzyme precursors, with inflammatory mediators, are released from the damaged pancreatic tissue and are capable of altering the function of the other organs, such as the lungs<sup>37,38</sup>. Acute pancreatitis due to scorpion is usually transient, self-limited and subsides until 48 h<sup>17,36</sup>, but it could progress to hemorrhagic pancreatitis and lead to death<sup>13</sup>.

Several laboratory abnormalities have been described in scorpion envenomation, including elevation of renal and pancreatic biomarkers, electrolytic disorders, hyperglycemia, coagulation disturbances<sup>17,20,21</sup>. In the present case, we have observed alterations in hematologic and coagulation parameters, such as increased glucose, AST and ALT levels. This may be due to the increased sympathetic activation and venom's toxic effects.

In this case, AKI was associated to scorpionism. There are few studies about AKI due to *T. stigmurus* and several pathophysiology mechanisms have been proposed to AKI in other scorpion accidents, including direct effect of venom on the kidney and renal damage due to intravascular hemolysis, disseminated intravascular coagulation and hypovolemia<sup>15</sup>. The highest concentration of scorpion venom is in the kidneys, mainly because of the fast redistribution of the venom from the blood to the tissues coupled with the slow removal of venom from the kidney<sup>39</sup>. Similarly, to the effects of *T. serrulatus* venom in human kidneys, in perfused rat kidneys, the renal perfusion pressure and the renal vascular resistance have increased, while the glomerular filtration rate has decreased, probably due to a direct vasoconstrictor action leading to a decreased renal flow<sup>39</sup>. Scorpion venom causes an inflammatory reaction in the kidneys<sup>23</sup>. The imbalance between inflammatory mediators and hypotensins<sup>23</sup> is decisive to damage the kidneys. Otherwise, Jalali *et al.*<sup>40</sup> reported children under 10 years old admitted to an intensive care unit following a sting from *Hemiscorpius lepturus* in Iran and revealed isolated hemoglobinuria with or without renal failure. In experimental studies about *H. lepturus* venom on rats, the main renal histopathological findings were morphological changes in the proximal tubular cell and glomerular network, besides focal necrosis and hemorrhage, with and without edema in lipid-containing organs such as liver, kidney and spleen<sup>40</sup>. Unfortunately, in the case reported here, urine tests were not requested.

The pathogenesis of AKI following a scorpion sting involves diverse mechanisms. Firstly, the occurrence of intravascular hemolysis, which could not appear in urine if it is mild and could vary according to the scorpion species<sup>41,42</sup>. In some species, the rhabdomyolysis, following extensive tissue necrosis, may cause pigment

nephropathy<sup>43</sup>. Haemoglobinuria could lead to AKI through multiple factors, such as mechanical obstruction by red blood cells casts, cytotoxic effects of oxidative stress induced by hemoglobin, heme, or iron released from red blood cells<sup>41,44</sup> and the worsening of renal vasoconstriction. Otherwise, vasodilation may lead to renal hypovolemia<sup>23</sup>. Finally, the antigen-antibody complexes may cause immune-complex glomerulonephritis, which require further immunofluorescent studies<sup>41</sup>. The direct toxic effect of venom could cause interstitial nephritis, release of cytokines and the vasodilatation may lead to ischemic tubular necrosis<sup>43</sup>. However, the renal failure is most likely not a direct nephrotoxic effect<sup>45</sup>, which remains to be investigated. Accordingly, some pathologic data from kidney biopsies revealed the association of these factors, such as direct nephrotoxicity of venom, haemoglobinuria, secondary to microvascular hemolysis and hypovolemia<sup>28,43</sup>.

Most reports about AKI due to scorpion stings are from Asia (Iran, Tunisia, Pakistan, Turkey and Israel)<sup>15,40,42,45-49</sup>, and are more common in pediatric patients, as summarized in Table 3. Most patients developed AKI in the setting of hypovolemia and cardiac failure, associated with acute tubular necrosis, pigmenturia, hemolytic uremic syndrome or interstitial nephritis, besides hemolysis<sup>15</sup>. In all studies it was highlighted that hemoglobinuria was useful to differentiate some species of scorpion in Iran<sup>42</sup>. Therefore, some authors suggested the use of urine analysis as a gold standard in the diagnosis of AKI following scorpion stings<sup>42</sup>.

Interestingly, the monocyte chemoattractant protein-1 (MCP-1) measured on admission, presented high levels, which represents an inflammatory process in the kidney and signalizes the risk of chronic injuries, considering that it has direct effects on monocytes and influences the migration, proliferation and differentiation of leukocytes<sup>2</sup>. In human renal tubular epithelial cells, MCP-1 stimulates interleukin-6 (IL-6) secretion and intercellular expression of adhesion molecule-1 (ICAM-1) synthesis. Furthermore, in podocytes, binding to the CC chemokine receptor 2 (CCR2) it could induce migration of podocytes and a significant reduction of both microRNA and protein expressions of nephrin<sup>50,51</sup>. This is an important scenario to understand the role of macrophages in renal abnormalities due to scorpion sting. It is imperative to emphasize the good performance of MCP-1 in our patient to detect AKI before abnormalities in creatinine, urinary neutrophil gelatinase-associated lipocalin (uNGAL) and kidney injury molecule-1 (KIM-1) collected about 5 hours after scorpion sting, even in a diabetic patient, who probably had kidney dysfunction because of her disease.

**Table 3** - Case reports of kidney involvement due to scorpion sting

References	Number of cases	Age <sup>a</sup>	Scorpion Specie	Initial presentation <sup>e</sup>	Antivenom	Pancreatic findings	Dialysis <sup>e</sup>	Outcome	Kidney findings <sup>e</sup>
Malhotra <i>et al.</i> , 1978 <sup>41</sup> , Iran	15 (9 males)	2.5 – 60 <sup>e</sup>	b	Local ulceration in stung site (3), hemoglobinuria, oliguria, edema, hemolytic anemia and hemolytic jaundice	No	b	Yes (5)	b	Hemoglobinuria, mesangial proliferation, variable degree of tubular changes and mild interstitial infiltration (4)
Chadha <i>et al.</i> , 1979 <sup>45</sup> , Iran	1 (female)	28	b	Bloody urine, breathless, severe hemolytic anemia, slight jaundice, puffy face, black necrotic area at the stung site, hypotension	Yes (dose did not report)		Yes	Discharge (skin grafting was performed later)	Hemoglobinuria, albuminuria, anuria (Not biopsied)
Naqvi <i>et al.</i> , 1998 <sup>47</sup> , Pakistan	1 (male)	60	b	Severe local pain, swelling (foot), hematuria, torpor, cervical rigidity	No	Normal amylase	Yes	Death (Disseminated intravascular coagulation and shock)	Hematuria, albuminuria, acute tubular necrosis in renal tissue
Derakhshan <i>et al.</i> , 2004 <sup>48</sup> , Iran	6	<16	b	Haemolysis	b	b	b	b	Acute tubular necrosis
Valavi <i>et al.</i> , 2008 <sup>49</sup> , India	1 (female)	7	<i>Hemiscorpius lepturus</i>	Bloody urine, vomiting, agitation, restlessness, erythematous area with local oedema at the stung site	Yes	b	Yes	Discharge in dialysis program	Hemoglobinuria, microscopic haematuria, proteinuria and erythrocyte casts, clinical diagnosis of haemolytic uremic syndrome (Not biopsied)
Jalali <i>et al.</i> , 2010 <sup>40</sup> , Iran	102	<10	<i>Hemiscorpius lepturus</i>	b	b	b	b	3 deaths (associated to AKI <sup>d</sup> )	Hemoglobinuria isolated (28) or with renal failure <sup>d</sup> (73)
Naqvi, 2015 <sup>43</sup> , Pakistan	18 (7 males)	10.74 – 47.7 <sup>c</sup>	b	Main stung site – foot, severe local pain, tingling, numbness, burning sensation, oliguria- anuria (16), haematuria/ hematemesis (10)	b	b	Yes (18)	16 discharge (13 with complete and 3 with partial renal recovery) and 2 deaths (cardiac arrhythmia and cardiomyopathy)	Haematuria (14), proteinuria (15), acute tubular necrosis and pigment casts without abnormal glomeruli (3)
Ranaweera <i>et al.</i> , 2015 <sup>28</sup> , Sri-Lanka	1	53	b	Vomiting, abdominal pain, haemoglobinuria progressing to anuria	No	b	Yes	Discharge in dialysis program (death 4 months later)	Haemorrhagic glomerular infarction with AKI
Vazirianzadeh <i>et al.</i> , 2017 <sup>42</sup> , Iran	103	≤14	<i>Hemiscorpius lepturus</i> and <i>Androctonus crassicauda</i>	b	b	b	b	4 deaths	Hemoglobinuria in different rates

a Years old; b Not reported; c Minimum – maximum; d Increase in serum creatinine or decrease in its clearance by more than 50% of standard values was considered as renal failure; e- number of patients with described characteristic were represented between parenthesis. \* Some scorpion species common in Pakistan: *Hemiscorpius lepturus*, *Mesobuthus tumulus*, *Androctonus crassicauda* and *M. eupeus*. \*\* Some scorpion species common in Iran (Khuzistan scorpions): genera *Buthus*, *Compsobuthus*, and *Hemiscorpius*, of which *Buthus sauloci* is the commonest.

The abdominal pain and laboratory findings were fundamental for the early diagnosis of acute pancreatitis and AKI in the patient, leading the physician to focus on the hemodynamic support in this case. Inasmuch there were drug treatment (with analgesics and antivenom), a multidisciplinary team composed of a nephrologist, a general clinician, a toxicologist chemist and nurses was essential to the outcome of our patient.

There are some limitations in this study including the lack of urinalysis and multiple analysis of kidney biomarkers to better clarify the pathophysiology of AKI in envenomations caused by *T. stigmurus* in humans. However, important findings that highlight scorpionism complications were described, and our patient's management may serve as guide in similar cases.

## CONCLUSION

Although envenomation cases due to *Tityus stigmurus* in Northeast Brazil and other tropical countries are often observed, severe manifestations are rare. Scorpion-related kidney injury and acute pancreatitis can occur in adults. The pathophysiology of AKI due to scorpionism is caused by multiple factors and the presence of blood in urine is one of the most common findings in the cases reported in the literature. The use of novel urinary biomarkers could be useful for the early diagnose of AKI in these accidents. Acute pancreatitis due to scorpionism have been reported mainly in children and could occur without increments of amylase and lipase. The diagnosis of systemic manifestation of envenomations due to scorpions, such as kidney and pancreatic injuries, is fundamental for the management of these patients.

## CONFLICT OF INTERESTS

All the authors declared no competing interests.

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