

1 Scorpion Sting and Acute Kidney Injury: Case Series from Pakistan

3 Abstract:

4 **Objectives:** We aim to report here a series of cases developing AKI after scorpion stings.

5 **Patients and Methods:** During a period of 25 years that is; from January 1990- December 2014
6 all the patients coming to Sindh Institute of Urology and Transplantation, with AKI after
7 scorpion sting are included in study. AKI was defined according to RIFLE criteria and Scorpion
8 sting was labeled on history of person stung by scorpion.

9 **Results:** During studied period 18 patients were brought with scorpion sting. Mean age of
10 patients was 29.22 ± 18.48 years, 7 were male and 11 females. Mean duration of insult was
11 8.94 ± 4.12 days. Sixteen out of 18 patients were either oliguric or anuric on presentation. Uremia
12 was advanced on arrival with mean urea of 324.38 ± 116.82 and creatinine of 11.8 ± 4.30 mg/dl.
13 Hyponatremia was a common finding with mean sodium of 129.16 ± 8.76 meq/l. Extensive tissue
14 damage at site of sting observed in many patients and mean values for LDH and CK were
15 2349.71 ± 3499.15 and 3116.23 ± 5468.22 U/L respectively. Hemodialysis required in all patients.
16 Complete renal recovery seen in 13 patients, 2 expired and 3 discharged from hospital in partial
17 state of recovery and never turned for follow up.

18 **Conclusion:** Scorpion sting is major health problem in many parts of our country, in majority it
19 takes a benign course but in some may affect multiple organs and result in death, especially if
20 initial treatment is delayed.

21 **Key Words:** AKI, RIFLE criteria, Scorpion Sting

23 Introduction:

24 There are about 2000 species of scorpion exist all over the world, most populated in warm and
25 dry tropical regions. In most species the sting is painful, but not fatal to humans. Approximately
26 25-40 species has been reported having toxins dangerous to human (1). More dangerous species
27 have been reported from Iran, Indian sub-continent, Turkey and Middle Eastern countries.
28 *Mesobuthus tumulus*, an Indian red scorpion is the most lethal species in India (2). While
29 *Hemiscorpius lepturus* most important from Iran, this species is endemic in Khuzestan and
30 south of Iraq (3). A dangerous and fatal species reported from United States is *Centruroides*
31 *exilicauda* or bark scorpion (1). The poison involved is mainly neurotoxin; but several
32 components including hemolysins, agglutinins, hemorrhagins, leucocytolysins, coagulins, lecithin
33 and cholesterol has been reported (4). Toxicity of venom is contributed by its proteolytic
34 content and phospholipases A₂, each venom contains 50-100 different polypeptides (5). The
35 renal injury may be caused by pigment nephropathy (myoglobin or hemoglobin pigment),
36 interstitial nephritis by direct toxin effect, rhabdomyolysis, intravascular hemolysis or

37 | vasculitis (5). [AKI may occur as part of multi organ failure in selected cases.](#)

38 The scorpion venom has been described to delay the closing of neuronal sodium channels,
39 resulting in “autonomic storm” this is because of sudden pouring of endogenous catecholamine
40 into the circulation. Autonomic storm is characterized by transient parasympathetic and
41 prolonged sympathetic stimulation (2).

42 Animal studies have shown induction of both pro and anti inflammatory cytokines after
43 exposure to venom (6). Reported renal pathologies are acute tubular necrosis, interstitial
44 nephritis, mesangial proliferation and hemolytic uremic syndrome (5,7,8,9,10). We aim to report
45 here a series of cases from our institution treated during last 25 years.

46

47 **Patients and Methods:**

48 This study is based on a series of 18 patients with AKI after scorpion sting from a retrospective
49 chart review of all patients admitted to the Sindh institute of Urology and Transplantation,
50 Karachi, Pakistan between January 1990 and December 2014. AKI was identified and staged
51 according to RIFLE criteria (11). Patients with preexisting kidney disease were excluded.
52 Diagnosis of scorpion sting was based on history of stung by scorpion, which was seen by
53 patient or close relative. Renal scan was done in all patients; those with normal size non
54 obstructed kidneys were included in study. Patients with other co-morbid were not included in
55 study.

56 Renal biopsy performed in three cases, and evaluated with light microscopy (LM) and immune
57 histochemistry. For LM, routinely 10 serial sections are cut and stained by hematoxylin and
58 eosin (H&E), Masson’s trichrome stain, periodic acid Schiff (PAS), and silver (Gomori’s
59 methenamine silver, GMS). While immune-histochemistry for myoglobin, tissue sections were
60 immersed in peroxidase quenching solution and rinsed with PBS. Primary antibody (polyclonal
61 rabbit anti human Myoglobin, Dako, Glostrup, Denmark) in dilution of 1:400 was applied for 30-
62 60 minutes at room temperature followed by PBS rinsing. Secondary antibody (HRP: horse
63 reddish peroxidase. Dako LSAB +/HRP kit, Dako, Glostrup, Denmark) was applied for 10
64 minutes at room temperature followed by PBS rinsing. Enzyme conjugate was applied for 10
65 minutes at room temperature followed by PBS rinsing. Chromogen substance (DAB,
66 Dako, Glostrup, Denmark) was applied for 5-10 minutes followed by PBS rinsing and light
67 counter stain with hematoxylin and mounting of slides.

68

69 All patients were followed up till death or complete renal recovery except 3 who lost follow up
70 after first discharge from hospital.

71

72 **Statistical methods:** Statistical analysis was done on SPSS version 15.0. Quantitative variables
73 reported as means \pm SD and Qualitative as percentages.

74

75 **Results:**

76 A total of 18 cases with AKI secondary to scorpion sting were registered during the study period.
77 There were 11 females and 7 males with mean age of 29.22 ± 18.48 years. Patients were brought
78 from different cities of Baluchistan province, distance was 323 – 585 km from Karachi in
79 southwestern direction. Fourteen (78%) cases were stung during months of summer which
80 extends from April to September in this region, and temperature ranges from 32 to 51°C during
81 these months.

82 Severe pain, tingling, numbness or burning sensation at site of sting was noticed in all of
83 patients. The second most common symptom was decline in urine output, reported in 89%
84 patients Table 1. Most frequent site was either foot in 6 cases, then thigh in 3, trunk 3, hand 2,
85 neck 2, pectoral region and forehead one each. Laryngeal edema and airway obstruction,
86 requiring mechanical ventilation, was noticed in one patient. Laboratory values of the day of
87 reporting at this hospital are given in Table 2, blood urea, serum creatinine, CK, LDH, were
88 increased several folds over the reference range, while AST and ALT were found mildly raised.
89 Hyponatremia was common with mean sodium of 129.16 ± 8.76 meq/l. Urinalysis was available
90 in 14 patients, dipstick revealed 1-3+ protein in 9 patients, while 1 had 4+ protein. Microscopy
91 revealed hematuria in 14 cases. Renal biopsy was performed in 3 patients;- revealed acute tubular
92 necrosis in all and pigment casts in 2; glomeruli were found to be normal. Two patients had
93 cardiac arrhythmias, one recovered and other died. Three patients had disturbed sensorium on
94 presentation with Glasgow coma scale 3-9.

95 Renal replacement therapy was required in all patients. Complete renal recovery occurred in
96 13(72.22%), while 2 died during acute phase of illness; the rest 3 lost for follow up after
97 discharge from the hospital. Those who expired; one was 60 years male who started recovering
98 renal functions, developed brady-arrhythmia and died of probably delayed cardiomyopathy.
99 While other who was 75 years female brought unconscious and died on same day of reaching to
100 this hospital. Photographs from necrotic lesion at site of sting, scorpion provided by one of
101 patient and renal biopsy from one patient are given here Fig. 1, 2 and 3.

102

103 **Discussion:**

104 In literature reported health hazards from scorpions are mostly from Iran, mid eastern countries,
105 Indian subcontinent, Mexico and North African Countries. Large epidemiology published from
106 Iran reports majority cases stung during summer and female affected more than male (12). We
107 have also noticed similarities in both, that is gender and season. *Hemiscorpius lepturus* is the
108 commonly reported scorpion species from the region where our studied patients belong. Others
109 reported are *Mesobuthus tumulus*, *Androctonus crassicauda*, and *M. eupeus* (16). Scorpion was
110 provided by one patient of present study population shown in Fig.1.

111 Pancreatitis after scorpion sting has been reported as early as 1970 (13), effect of toxin studied
112 on animal cardiac muscle reported in 1974 (14), then human studies on cardiac dysfunction and
113 pulmonary edema in literature from Israel, states that cardiac injury persisted for prolonged
114 duration (15). One of our patients who died after 15 days of scorpion sting while already

115 recovering from renal failure could be due to delayed cardiomyopathy as he developed brady
116 arrhythmia and hypotension at this late stage. A series of cases developing renal injury first
117 reported by Malhotra et al in 1978 (8), later isolated cases are found in literature, we have also
118 reported one case from present cohort previously in 1998 (7). Renal injury in these patients may
119 result from intravascular hemolysis, rhabdomyolysis after extensive tissue necrosis, both may
120 cause pigment nephropathy. Then direct toxic effect of venom may cause interstitial nephritis,
121 release of cytokines and vasodilatation may lead to ischemic tubular necrosis. Furthermore,
122 “autonomic storm” may lead to shock and renal cortical necrosis. In present study we have found
123 evident acute tubular necrosis and pigment nephropathy, while we are uncertain about interstitial
124 nephritis and acute cortical necrosis as we have not performed renal biopsy in all and then 3 of
125 our patients lost follow up and in them we are not sure whether they recovered or developed
126 chronic kidney disease.

127 Stung on trunk and neck allow more venom to reach the blood and thus cause more morbidity
128 half of our patients had stung in these regions. Pain at site of sting, numbness and tingling
129 sensations are commonly described symptoms (1,2,7,8) and reported by all of our patients.
130 Similarly decline in urine output from oliguria to absolute anuria is also well reported entity
131 (5,7,8) and found in 89 % of present study population. Local manifestation vary from no sign
132 other than mild edema to ecchymosis, extensive cellulites and necrosis (16,17), in our studied
133 population 61% patients had these findings, tissue necrosis was extensive in 3 patients, and
134 required skin grafting in later stage(Fig.2). Area involved around site ranged from 50-2000mm in
135 these patients, available photograph is from patient who had medium size necrotic area. High
136 levels of muscle enzymes i.e; LDH, CK and AST can be explained with extensive tissue damage
137 at site of sting. Hyponatremia has been reported in one case by Chadah et al (17) and
138 hypernatremia one case by Derakhshan et al (10) in past studies, in our study average patients
139 had low serum sodium levels. We could not measure fractional excretion of sodium (FeNa) in
140 our patients, 4 patients had absolute anuria, and some reached late to this hospital. Thus we are
141 not in position to comment on renal handling of sodium in these cases from our own experience.

142 Malhotra et al in their case series performed renal biopsy in 4 patients and reported mesangial
143 proliferation, variable degree of tubular damage and mild interstitial inflammation. We have
144 done renal biopsy in 3 and find acute tubular necrosis in all with presence of pigment casts in
145 tubular lumina in one case. Pigment was myoglobin as proved by immune histochemistry
146 (Fig.3).

147 **Limitations:** FeNa was not available in our studied population and majority patients had low
148 serum sodium but we cannot comment on renal handling of sodium in these patients.

149 **Conclusion:** Scorpion sting is important issue to address in parts of country where poisonous
150 species inhabitants. Fatal complications may occur at early as well as late after sting. Those who
151 get delay in starting treatment are more prone to develop complications.

152

153 **References:**

- 154 1. http://www.emedicinehealth.com/wilderness_scorpion_sting/article_em.htm#scorpion_sting_o
155 [verview](#)
156 Accessed 28th may 2015
- 157 2. Bawaskar HS, Bawaskar PH; Efficacy and safety of scorpion antivenom plus prazosin
158 compared with prazosin alone for venomous scorpion (*Mesobuthus tamulus*) sting:
159 randomised open label clinical trial. *BMJ* 2010;341:c7136
- 160 3. Valavi E, Ansari MJA, Hoseini S; ADAMTS-13 Deficiency following *Hemiscorpius*
161 *lepturus* Scorpion Sting. *Saudi J of Kidney Dis Transpl.* 2011,22 (4):792-5.
162
- 163 4. In Modi's Text Book of Medical jurisprudence and Toxicology. Ed N.J. Modi, 19th Ed.
164 1977, Publisher N. M. Tripathi, Bombay, India. P 636.
165
- 166 5. Viswanathan S , PrabhuC; Scorpion sting nephropathy. *NDT Plus*, 2011, 4: 376– 82
- 167 6. Petricevich VL. Scorpion venom and the inflammatory response. *Mediators Inflamm*
168 2010; 2010: 903295
- 169 7. Naqvi R, Naqvi A, Akhtar F, Rizvi A; Acute renal failure developing after a scorpion
170 sting. *Br J Urol* 1998; 82: 295.
- 171 8. Malhotra KK, Mirdehghan CM, Tandon HD. Acute renal failure following scorpion
172 sting. *Am J Trop Med Hyg* 1978; 27: 623– 6
173
174
- 175 9. Mocan H, Mocan MZ, Kaynar K. Haemolytic-uraemic syndrome following a scorpion
176 sting. *Nephrol Dial Transplant* 1998; 13: 2639–2640
- 177 10. Derakhshan A, Al Hashemi GH, Fallahzadeh MH. Spectrum of inpatient renal disease in
178 children: ‘‘ A Report from Southern part Islami Republic of Iran’’. *Saudi J Kidney Dis*
179 *Transplant* 2004; 15: 12–17
180
181
- 182 11. Lameire N, Van Biesen W, Vanholder R; Acute Renal Failure. *Lancet*, 2006,
183 365(9457):417-30.
184
- 185 12. Karami K, VazirianzadehB , Mashhadi E, Hossienzadeh M , Moravvej SA; A Five Year
186 Epidemiologic Study on Scorpion Stings in Ramhormoz, South-West of Iran. *Pakistan J.*
187 *Zool.*2013, vol. 45(2), pp. 469-74.
188
- 189 13. Bartholowmew C; Acute Scorpion Pancreatitis in Trinidad. *BMJ.* 1970,I 666-8.
190
- 191 14. Freire-Maia L, Pinto GL, Franco I; Mechanism of cardio vascular effects produced by
192 purified scorpion toxin in rats. *J of Phatmacol and Experim Therapeut.* 1974, 188, 207-
193 13.
194

195 15. Rahav G, Weiss AT; Scorpion sting induced pulmonary edema. Scintigraphic evidence of
 196 cardiac dysfunction. Chest 1990, 97 (6):1478-80.
 197
 198 16. Radmanesh M; Clinical study of Hemiscorpion lepturus in Iran. J Trop Med and Hyg.
 199 1990, 93:327-32.
 200
 201 17. Chadha JS, Leviav A; Hemolysis, Renal Failure and Local Necrosis Following Scorpion
 202 Sting. JAMA, 1979, 241 (10):1038.
 203

204 **Table1: Clinical Parameters of Patients (N=18)**

Parameter	numbers	%
Local pain, numbness, tingling	18	100
Oligo-anuria	16	88.88
Local ecchymosis, cellulites, necrosis	11	61.11
Hematuria/ hemetamesis	10	55.55
Drowsiness/ altered sensorium	4	22.22

205

206 **Table 2: Laboratory Parameters of Patients (N=18)**

Parameters	mean±SD
Hb (g/dl)	7.6±3.04
Urea (mg/dl)	324.38±116.82
Serum Creatinine (mg/dl)	11.8±4.30
Serum Sodium	129.16±8.76
Serum Potassium (meq/l)	4.9±1.24
LDH (U/L)	2349.71±3499.15
CK (U/L)	3116.23±5468.22
AST (U/L)	91.56±158.75
ALT (U/L)	65.93±79.79
Proteinuria on dipstick (%)	55.55
Micrpsopic hematuria (%)	77.77

207



208

209 Fig. 1: Scorpion provided by one patient included in cohort.

210



211

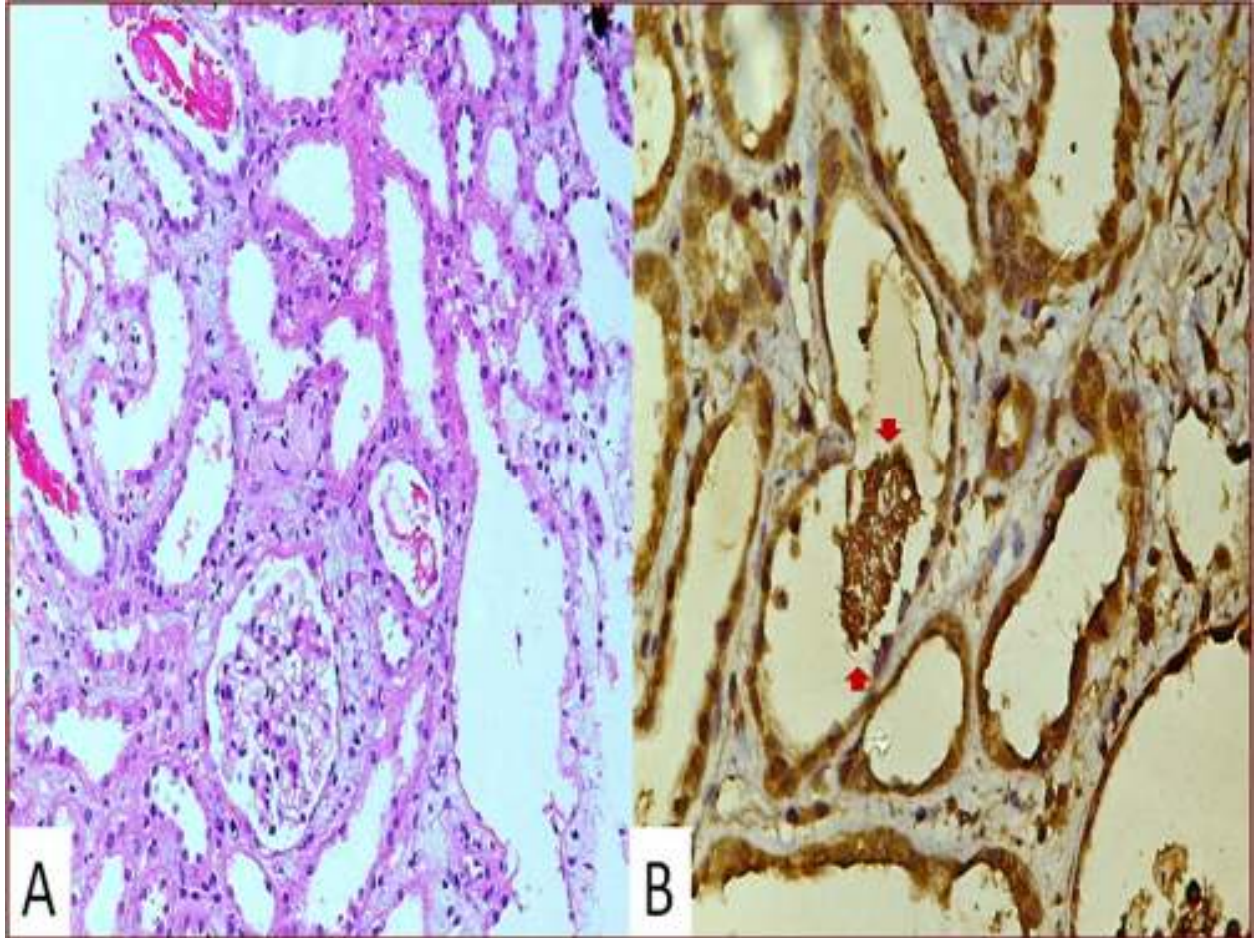
212 Fig. 2- Site of Scorpion Sting, local necrosis.

213

214

215

216



217
218
219
220

Fig 3: A- Light Microscopy. H and E stain, showing ATN and pigment casts in some lumina.
B. Immune histochemistry, positive staining of pigment cast for myoglobin, tubules show non specific staining..