

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

2

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.

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

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22 Introduction:

23 There are about 2000 species of scorpion exist all over the world, most populated in warm and
24 dry tropical regions. In most species the sting is painful, but not fatal to humans. Approximately
25 25-40 species has been reported having toxins dangerous to human (1). More dangerous species
26 have been reported from Iran, Indian sub-continent, Turkey and Middle Eastern countries.
27 *Mesobuthus tumulus*, an Indian red scorpion is the most lethal species in India (2). While
28 *Hemiscorpius lepturus* most important from Iran, this species is endemic in Khuzestan and
29 south of Iraq (3). A dangerous and fatal species reported from United States is *Centruroides*
30 *exilicauda* or bark scorpion (1). The poison involved is mainly neurotoxin; but several
31 components including hemolysins, agglutinins, hemorrhagins, leucocytolysins, coagulins, lecithin
32 and cholesteroin has been reported (4). Toxicity of venom is contributed by its proteolytic
33 content and phospholipases A₂, each venom contains 50-100 different polypeptides (5).
34 Autonomic stimulation occurs after envenomation. Animal studies have shown induction of both

35 pro and anti inflammatory cytokines after exposure to venom (6). Reported renal pathologies are
36 acute tubular necrosis, interstitial nephritis, mesangial proliferation and hemolytic uremic
37 syndrome (5,7,8,9,10). We aim to report here a series of cases from our institution treated during
38 last 25 years.

39

40 **Patients and Methods:**

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

49 Renal biopsy performed in three cases, and evaluated with light microscopy (LM) and immune
50 histochemistry. For LM, routinely 10 serial sections are cut and stained by hematoxylin and
51 eosin (H&E), Masson's trichrome stain, periodic acid Schiff (PAS), and silver (Gomori's
52 methenamine silver, GMS). While immune-histochemistry for myoglobin, tissue sections were
53 immersed in peroxidase quenching solution and rinsed with PBS. Primary antibody (polyclonal
54 rabbit anti human Myoglobin, Dako, Glostrup, Denmark) in dilution of 1:400 was applied for 30-
55 60 minutes at room temperature followed by PBS rinsing. Secondary antibody (HRP: horse
56 reddish peroxidase. Dako LSAB +/HRP kit, Dako, Glostrup, Denmark) was applied for 10
57 minutes at room temperature followed by PBS rinsing. Enzyme conjugate was applied for 10
58 minutes at room temperature followed by PBS rinsing. Chromogen substance (DAB,
59 Dako, Glostrup, Denmark) was applied for 5-10 minutes followed by PBS rinsing and light
60 counter stain with hematoxylin and mounting of slides.

61

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

64

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

67

68 **Results:**

69 A total of 18 cases with AKI secondary to scorpion sting were registered during the study period.
70 There were 11 females and 7 males with mean age of 29.22 ± 18.48 years. Patients were brought
71 from different cities of Baluchistan province, distance was 323 – 585 km from Karachi in
72 southwestern direction. Fourteen (78%) cases were stung during months of summer which
73 extends from April to September in this region, temperature ranges from 32 to 44⁰C.

74 Severe pain, tingling, numbness or burning sensation at site of sting was noticed in all of
75 patients. The second most common symptom was decline in urine output, reported in 89%
76 patients Table 1. Most frequent site was either foot in 6 cases, then thigh in 3, trunk 3, hand 2,
77 neck 2, pectoral region and forehead one each. Laryngeal edema and airway obstruction,
78 requiring mechanical ventilation, was noticed in one patient. Laboratory values of the day of
79 reporting at this hospital are given in Table 2, blood urea, serum creatinine, CK, LDH, were
80 increased several folds over the reference range, while AST and ALT were found mildly raised.
81 Hyponatremia was common with mean sodium of 129.16 ± 8.76 meq/l. Urinalysis was available
82 in 14 patients, dipstick revealed 1-3+ protein in 9 patients, while 1 had 4+ protein. Microscopy
83 revealed hematuria in 14 cases. Renal biopsy was performed in 3 patients it revealed acute
84 tubular necrosis in all 3 and pigment casts in 2; glomeruli were found to be normal. Renal
85 replacement therapy was required in all patients. Complete renal recovery occurred in
86 13(72.22%), while 2 died during acute phase of illness; the rest 3 lost for follow up after
87 discharge from the hospital. Those who expired; one was 60 years male who started recovering
88 renal functions, developed brady-arrhythmia and died of probably delayed cardiomyopathy.
89 While other who was 75 years female brought unconscious and died on same day of reaching to
90 this hospital. Photographs from necrotic lesion at site of sting, scorpion provided by one of
91 patient and renal biopsy from one patient are given here Fig. 1, 2 and 3.

92

93 **Discussion:**

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

101 Pancreatitis after scorpion sting has been reported as early as 1970 (13), effect of toxin studied
102 on animal cardiac muscle reported in 1974 (14), then human studies on cardiac dysfunction and
103 pulmonary edema in literature from Israel, states that cardiac injury persisted for prolonged
104 duration (15). One of our patients who died after 15 days of scorpion sting while already
105 recovering from renal failure could be due to delayed cardiomyopathy as he developed brady
106 arrhythmia and hypotension at this late stage. A series of cases developing renal injury first
107 reported by Malhotra et al in 1978 (8), later isolated cases are found in literature, we have also
108 reported one case from present cohort previously in 1998 (7).

109 Stung on trunk and neck allow more venom to reach the blood and thus cause more morbidity
110 half of our patients had stunged in these regions. Pain at site of sting, numbness and tingling
111 sensations are commonly described symptoms (1,2,7,8) and reported by all of our patients.
112 Similarly decline in urine output from oliguria to absolute anuria is also well reported entity

113 (5,7,8) and found in 89 % of present study population. Local manifestation vary from no sign
 114 other than mild edema to ecchymosis, extensive cellulites and necrosis (16,17), in our studied
 115 population 61% patients had these findings, tissue necrosis was extensive enough in 3 patients, to
 116 require skin grafting later on (Fig.2). Area involved around site ranged from 50-2000mm. High
 117 levels of muscle enzymes i.e; LDH, CK and AST can be explained with extensive tissue damage
 118 at site of sting. Hyponatremia has been reported in one case by Chadah et al (17) and
 119 hypernatremia one case by Derakhshan et al (10) in past studies, in our study average patients
 120 had low serum sodium levels. We could not measure fractional excretion of sodium (FeNa) in
 121 our patients, 4 patients had absolute anuria, and some reached late to this hospital. Thus we are
 122 not in position to comment on renal handling of sodium in these cases from our own experience.

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

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

130 **Conclusion:** Scorpion sting is important issue to address in parts of country where poisonous
 131 species inhabitants. Fatal complications may occur at early as well as late after sting.

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133 **References:**

- 134 1. http://www.emedicinehealth.com/wilderness_scorpion_sting/article_em.htm#scorpion_sting_o
 135 [view](http://www.emedicinehealth.com/wilderness_scorpion_sting/article_em.htm#scorpion_sting_o)
 136 Accessed 28th may 2015
- 137 2. Bawaskar HS, Bawaskar PH; Efficacy and safety of scorpion antivenom plus prazosin
 138 compared with prazosin alone for venomous scorpion (*Mesobuthus tamulus*) sting:
 139 randomised open label clinical trial. *BMJ* 2010;341:c7136
- 140 3. Valavi E, Ansari MJA, Hoseini S; ADAMTS-13 Deficiency following *Hemiscorpius*
 141 *lepturus* Scorpion Sting. *Saudi J of Kidney Dis Transpl.* 2011,22 (4):792-5.
 142
- 143 4. In Modi's Text Book of Medical jurisprudence and Toxicology. Ed N.J. Modi, 19th Ed.
 144 1977, Publisher N. M. Tripathi, Bombay, India. P 636.
 145
- 146 5. Viswanathan S , PrabhuC; Scorpion sting nephropathy. *NDT Plus*, 2011, 4: 376– 82
- 147 6. Petricevich VL. Scorpion venom and the inflammatory response. *Mediators Inflamm*
 148 2010; 2010: 903295
- 149 7. Naqvi R, Naqvi A, Akhtar F, Rizvi A; Acute renal failure developing after a scorpion
 150 sting. *Br J Urol* 1998; 82: 295.

151 8. Malhotra KK, Mirdehghan CM, Tandon HD. Acute renal failure following scorpion
 152 sting. *Am J Trop Med Hyg* 1978; 27: 623– 6
 153
 154
 155 9. Mocan H, Mocan MZ, Kaynar K. Haemolytic-uraemic syndrome following a scorpion
 156 sting. *Nephrol Dial Transplant* 1998; 13: 2639–2640
 157 10. Derakhshan A, Al Hashemi GH, Fallahzadeh MH. Spectrum of inpatient renal disease in
 158 children: “ A Report from Southern part Islami Republic of Iran”. *Saudi J Kidney Dis*
 159 *Transplant* 2004; 15: 12–17
 160
 161
 162 11. Lameire N, Van Biesen W, Vanholder R; Acute Renal Failure. *Lancet*, 2006,
 163 365(9457):417-30.
 164
 165 12. Karami K, VazirianzadehB , Mashhadi E, Hossienzadeh M , Moravvej SA; A Five Year
 166 Epidemiologic Study on Scorpion Stings in Ramhormoz, South-West of Iran. *Pakistan J.*
 167 *Zool.*2013, vol. 45(2), pp. 469-74.
 168
 169 13. Bartholowmew C; Acute Scorpion Pancreatitis in Trinidad. *BMJ*. 1970,I 666-8.
 170
 171 14. Freire-Maia L, Pinto GL, Franco I; Mechanism of cardio vascular effects produced by
 172 purified scorpion toxin in rats. *J of Phatmacol and Experim Therapeut.* 1974, 188, 207-
 173 13.
 174
 175 15. Rahav G, Weiss AT; Scorpion sting induced pulmonary edema. Scintigraphic evidence of
 176 cardiac dysfunction. *Chest* 1990, 97 (6):1478-80.
 177
 178 16. Radmanesh M; Clinical study of Hemiscorpion lepturus in Iran. *J Trop Med and Hyg.*
 179 1990, 93:327-32.
 180
 181 17. Chadha JS, Leviav A; Hemolysis, Renal Failure and Local Necrosis Following Scorpion
 182 Sting. *JAMA*, 1979, 241 (10):1038.
 183

184 **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

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186 **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

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

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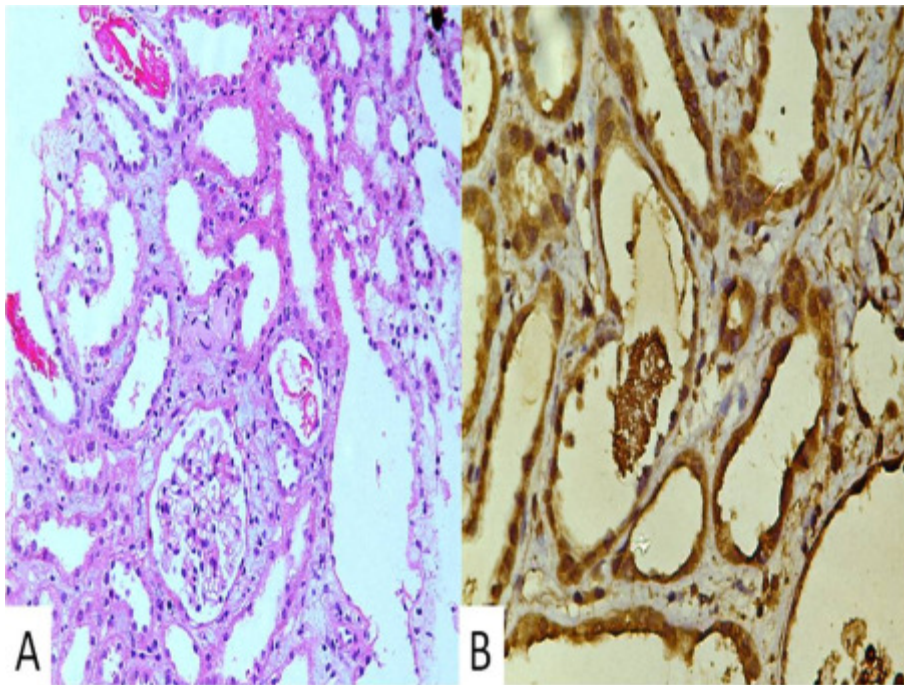


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192 Fig. 2- Site of Scorpion Sting, local necrosis.

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197 Fig 3: A- Light Microscopy. H and E stain, showing ATN and pigment casts in some lumina.

198 B. Immune histochemistry, positive staining of pigment cast for myoglobin.