# **Research Article**

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# Autonomic dysfunctions in patients with scorpion sting: early predictors of severe disease

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#### **ABSTRACT**

**Background:** Scorpion sting envenomation is a common medical emergency accounting for nearly 2.8% of annual intensive cardiac care unit admissions and much more outpatient visits. Symptomatology and severity of envenomation varies greatly. Autonomic storm may end up in loss of life.

**Methods:** This is a clinical study conducted between April 2011 and February 2013. Patients with moderate to severe envenomation were examined at frequent intervals for various autonomic manifestations. Various demographic, clinical and electrocardiogram (ECG) changes were studied for their association with severity of envenomation. Results were statistically evaluated for their significance.

**Results:** A total of 106 patients were studied with a mean age of 27.25 years and peak incidence between 11 and 30 year age groups. 91% reached the hospital within 12 h. 7.55% of the patients had Grade 2, 74.53% had Grade 3 and 17.92% had Grade 4 disease, all grades were common in 11-30 age group. Autonomic disturbances; profuse sweating seen in 72.6% of the patients that showed a strong correlation with pulmonary edema and ECG manifestations ( $p \le 0.0001$ ). Pulmonary edema was present in 37.7% of the patients. Excessive salivation was seen in 28.3%, and persistent nausea and vomiting were seen in 24.5%, both were associated with severe cardio-pulmonary manifestations. Hypotension was present in 14.2% of patients that was associated with poor prognosis ( $p \le 0.0001$ ).

**Conclusions:** Scorpion sting envenomation is a life-threatening problem requiring immediate attention. Presence of autonomic dysfunctions; profuse sweating, excessive salivation, persistent nausea and vomiting, hypotension at presentation are poor prognostic factors.

Keywords: Scorpion sting, Autonomic storm, Autonomic dysfunction, Prognostic indicators

## INTRODUCTION

Scorpion envenomation is a major health problem in tropical and subtropical countries, the fact that many of these areas are underdeveloped, problem is not properly assessed and the consequences are under-reported owing to poor medical and statistical facilities.<sup>1,2</sup> Due to above reasons the true incidence of this common rural, to some extent on occupational hazard is not known.<sup>2</sup>

There are about 1500 scorpion species worldwide, 50 are dangerous to humans. Almost all of lethal scorpion belongs

to Buthide family.<sup>3</sup> There are about 86 species of scorpions found in India,<sup>1,2</sup> only three of them are poisonous, they include;<sup>1</sup> *Mesobuthus tumulus, Palamneus swammerdami* and *Heterometrus bengalensis*.

Two most commonly found species in and around our study area are, the *Buthus tamulus*; Adults of *B. tamulus* measure about 7-9 cm in length, reddish yellow in color. It is frequently found in houses and its venom is more toxic, particularly cardio-toxic<sup>2,4-6</sup> and *Palamneus swammerdami*; The adults measure up to 15 cm in length, blackish in color, and are found on the hills and shrubby areas. Its venom is less toxic.<sup>4,6</sup>

We studied the autonomic effects of Indian red scorpion, *B. tamulus*, which is widely prevalent and highly toxic with median lethal dose of 3.5 mg with the objectives to study the various autonomic manifestations and to assess the early clinical features for their probable association with subsequent development of severe disease.

## **METHODS**

This cross-sectional study was undertaken in medical Intensive Care Unit (ICU), and medical wards in the Department of Medicine. A total of 786 patients with scorpion sting visited VIMS Hospital during the period of 22 months of the study. Of them, only 106 patients with moderate to severe envenomation were included in the study. All patients with a history of scorpion sting were subjected to thorough clinical examination to assess various systemic manifestations with special attention to autonomic manifestations at admission, after 1 h and 6 h and subsequently depending on the need. For the purpose of the study, cases were allocated into four groups according to the severity of envenomation they include Grade 1 to Grade 4.

Patients with Grade 1 disease were discharged after symptomatic therapy and were not included in the study. Patients with Grade 3 and Grade 4 envenomation were admitted in ICU ward and those with Grade 2 envenomation were admitted in medical emergency department. All cases were asked detailed history and subjected to thorough clinical examination particularly for autonomic manifestations. All the patients were subjected to necessary investigations.

Demographic features such as age, sex, time since sting to the arrival to the hospital and clinical parameters like pain at the site of sting, swelling, parasthesia, profuse sweating, excessive salivation and hypotension and priapism and electrocardiogram (ECG) changes were studied for association with subsequent development of signs of severe envenomation.

All patients were received tetanus toxoid depending on immunization status. All patients with local pain were treated with 2% xylocaine local infiltration and repeated if necessary. All were treated with tablet prazosin, except those with hypotension. Intravenous fluids, diuretics,  $O_2$  inhalation, and inotropic supports were given whenever required.

Access to scorpion antivenom as changed the overall approach to the management of scorpion envenomation. However, unfortunately we could not use the antivenom as it is currently not available at our institution.

Patients were followed up at regular intervals, at 1 h, 6 h, 12 h, 24 h, and 48 h and if necessary till the patients were discharged from the hospital.

All patient profiles were recorded in the proforma, entered into master chart, and findings were tabulated and subjected to appropriate statistical analysis. Statistical tests used in this study are Chi-square test, ANOVA-without replication, and Student t-test.

#### RESULTS

A total of 106 patients with systemic manifestations constituted the study sample.

Table 1 shows the age and sex distribution.

Mean age for all patients is 27.25 years (males 28 years and females 25.76 years). Scorpion sting was more commonly seen in the age group of 11-30 years, accounting for 68.87% of the patients (73 cases).

All grades of envenomation were common in the age group of 11-30 years with 73 (68.87%) patients belonging to this age group. Out of 106 patients, 74.5% (79) patients had grade 3 disease, about 17.92% (19) of patients had Grade 4 disease, and only 7.55% of the patients had Grade 2 envenomation. About 81.9% (59) of the males and 58.8% (20) of the females had Grade 3 envenomation, accounting for a total of 74.53%. About 12.5% of the males and 29.4% of the females were in Grade 4 envenomation. Remaining 7.55% had Grade 2 envenomation.

More than half of patients (51%) reached hospital within 6 h, another 47.2% within 24 h. Only 2 patients reached hospital after 24 h.

Table 2 shows the distribution of the patients according to the common presenting symptoms. Pain was most common clinical presentation of the patients (99.1%) with scorpion sting. About 98.6% of the males and all females had pain

Table 1: Age and sex distribution of scorpion sting cases.

Age	Grade 2		Grade 3		Grade 4	Grade 4		Total	
group	Male	Female	Male	Female	Male	Female	Male	Female	
11-20	2 (1.9)	3 (2.8)	21 (19.8)	8 (7.5)	4 (3.8)	7 (6.6)	27 (25.5)	18 (17.0)	
21-30	2 (1.9)	1 (0.9)	14 (13.2)	7 (6.6)	3 (2.8)	1 (0.9)	19 (17.9)	9 (8.5)	
31-40	0	0	12 (11.3)	3 (2.8)	0	0	12 (11.3)	3 (2.8)	
41-50	0	0	10 (9.4)	0	0	0	10 (9.4)	0	
51-60	0	0	1 (0.9)	1 (0.9)	2 (1.9)	1 (0.9)	3 (2.8)	2 (1.9)	
61-70	0	0	1 (0.9)	1 (0.9)	0	1 (0.9)	1 (0.9)	2 (1.9)	
Total	4 (3.8)	4 (3.8)	59 (55.7)	20 (18.9)	9 (8.5)	10 (9.4)	72 (67.9)	34 (32.1)	

at the site of the bite. It was followed by cold peripheries (48.1%), paraesthesia (44.3%), swelling (42.5%), cough (40.6%), breathlessness (38.7%), LVS3 (34%) in majority of the patients.

Table 3 shows the autonomic abnormalities in the patients. Tachycardia (86.8%) was most common autonomic feature in the study group.

The difference in features between the sexes was noticed in sweating, tachypnea, hypertension, nausea/vomiting and palpitation.

The common sympathetic features noticed were tachycardia (86.8%), Profuse sweating (72.6%), hypertension (43.4%), palpitation (18.7%), pulmonary edema (37.7%), mydriasis (23.6%) and piloerection (21.7%).

Most common parasympathetic features were bradycardia, hypotension (14.2%) excessive salivation (28.3%), bronchoconstriction (13.2%), miosis (4.7%), priapism (13.2%), and dysphagia (4.7%).

Table 4 shows the distribution of autonomic abnormalities across the grades of envenomation.

#### DISCUSSION

This cross-sectional study was undertaken with the aim of studying autonomic abnormalities in patients with moderate

Table 2: Common clinical features of scorpion envenomation.

Clinical features	Number (%)				
	Male (n=72)	Female (n=34)	Total ( <i>n</i> =106)		
Pain	71 (98.6)	34 (100)	105 (99.1)		
Cold peripheries	31 (43.1)	20 (58.8)	51 (48.1)		
Paraesthesia	32 (44.4)	15 (44.1)	47 (44.3)		
Swelling	28 (38.9)	17 (50)	45 (42.5)		
Cough	24 (33.3)	19 (55.9)	43 (40.6)		
Breathlessness	21 (29.2)	20 (58.8)	41 (38.7)		
Pulmonary edema	23 (31.9)	17 (50)	40 (37.7)		
LVS3	19 (26.4)	17 (50)	36 (34)		
Giddiness	15 (20.8)	7 (20.6)	22 (20.8)		
Altered sensorium	9 (12.5)	10 (29.4)	19 (17.9)		
Bronco-constriction	6 (8.33)	8 (23.5)	14 (13.2)		
Hemoptysis	6 (8.33)	7 (20.6)	13 (12.3)		
Blurring of vision	9 (12.5)	4 (11.8)	13 (12.3)		
Murmur	6 (8.33)	6 (17.6)	12 (11.3)		
Pain abdomen	9 (12.5)	2 (5.9)	11 (10.4)		
Abdominal tenderness	2 (2.8)	5 (14.7)	7 (6.6)		
Focal deficits	3 (4.2)	0	3 (2.8)		

to severe scorpion sting envenomation. 106 patients passed the eligibility criteria for the study during our study period of 22 months prospectively. Scorpion sting envenomation is relatively common medical emergency at our institution accounting for nearly 400 emergency department visits annually. About 13.48% of total scorpion sting victims required ICU admission, amounting to 10% of the total ICU bed occupancy reflects the magnitude of the problem.

As the department does not have access to pediatric patients, those aged <10 years were excluded from the study. Age of the patients in this study ranged from 12 to 64 years, with a mean age of envenomation 27.3 years. About 68.9% of the patients were in the age group of 11-30 years, as this age group is productive, have increased the risk of scorpion envenomation that is purely an accidental phenomenon. Same reason also explains that the problem was common in males due to increased outdoor activities especially during morning and evening hours.

Majority of the patients had sting during the early morning (48%) and (38%) evening hours. This correlates with the maximum activity of people during these hours; scorpions are also more active during these hours. Cheng et al. also noticed the same.<sup>3</sup>

Ninety-seven patients in this study presented to the emergency department within 12 h (91%). There was no statistical correlation between the time lag in attending to emergency department and severity of envenomation. In the contrary to the present study previous studies by Bawaskar and Bawaskar, and Mahadevan reported that the delay in hospital presentation was associated with severe manifestation.<sup>2,4,5</sup> This may be due to milder

Table 3: Autonomic abnormalities in the study group.

Clinical features	Number (%)				
	Male (n=72)	Female (n=34)	Total		
Tachycardia	59 (81.9)	33 (97.1)	92 (86.8)		
Profuse sweating	50 (69.4)	27 (79.4)	77 (72.6)		
Tachypnea	33 (45.8)	18 (52.9)	51 (48.1)		
Hypertension	33 (45.8)	13 (38.2)	46 (43.4)		
Excess salivation	20 (27.8)	10 (29.4)	30 (28.3)		
Nausea/vomiting	16 (22.2)	10 (29.4)	26 (24.5)		
Mydriasis	17 (23.6)	8 (23.5)	25 (23.6)		
Piloerection	16 (22.2)	7 (20.6)	23 (21.7)		
Palpitation	11 (15.3)	9 (26.5)	20 (18.7)		
Hypotension	10 (13.9)	5 (14.7)	15 (14.2)		
Priapism	14 (19.4)	0	14 (13.2)		
Bradycardia	7 (9.7)	0	7 (6.6)		
Carpopedal spasm	4 (5.6)	3 (8.8)	7 (6.6)		
Dysphagia	3 (4.12)	2 (5.9)	5 (4.7)		
Miosis	4 (5.6)	1 (2.9)	5 (4.7)		

Table 4: Autonomic abnormalities across grades of envenomation.

Autonomic	Number (%)					
abnormality	Grade II (n=8)	Grade III (n=79)	Grade IV (n=19)	Total (n=106)		
Tachycardia	7 (87.5)	66 (83.5)	19 (100)	92 (86.8)		
Profuse sweating	0 (0)	59 (74.7)	18 (94.7)	77 (72.6)		
Tachypnea	3 (37.5)	33 (41.8)	15 (78.9)	51 (48.1)		
Excess salivation	0 (0)	25 (31.6)	5 (26.3)	30 (28.3)		
Nausea/vomiting	0 (0)	21 (26.6)	5 (26.3)	26 (24.5)		
Mydriasis	1 (12.5)	18 (22.8)	6 (31.6)	25 (23.6)		
Piloerection	1 (12.5)	19 (24.1)	3 (15.8)	23 (21.7)		
Palpitation	2 (25)	14 (17.7)	4 (21)	20 (18.7)		
Hypotension	0 (0)	10 (12.7)	5 (26.3)	15 (14.2)		
Priapism	0 (0)	11 (13.9)	3 (15.8)	14 (13.2)		
Bradycardia	0 (0)	7 (8.9)	0 (0)	7 (6.6)		
Carpopedal spasm	0 (0)	6 (7.6)	1 (5.3)	7 (6.6)		
Dysphagia	0 (0)	2 (2.5)	3 (15.8)	5 (4.7)		
Miosis	0 (0)	5 (6.3)	0 (0)	5 (4.7)		

case presented to the hospital only when there was no relief of symptoms but most of the moderate to severe envenomation presented relatively early because of early development of annoying symptoms. Accessibility may be the other factor which may result in delayed presentation of the cases to the hospital.

Seventy-two patients had sting over distal parts of upper limbs, 24 patients had stings over lower limbs, 7 patients had over trunk and they also had stung over other parts. There was no association between site of sting and severity of envenomation.

All grades of envenomation were common in the age group of 11-30 years accounting for 69% of the cases. This can be due to a higher number of cases in this age group. However, ANOVA: two-factor without replication shows significant association between severity of envenomation and age with p value of 0.046 for different ages and 0.005 for different grades of the disease. Previous studies say that younger age is associated with more severe disease, but we could not test this hypothesis as we excluded cases below 12 years. In this study, 72 patients were males, and 34 were females. 82% of the males and 59% of the females had Grade 3 disease. However, there was no statistically significant association between different grades of envenomation with either of the sex (p=0.26) or different grades in the same sex (p=0.44).

Pain was present in 105 (99.06%) patients, which was the most common presentation.<sup>2,4,5,7,8</sup> It is noted from the study that those with severe pain at presentation had relatively milder systemic manifestation and majority of patients with severe envenomation had mild pain, this finding is in accordance with the findings of Bawaskar and Bawaskar, Mahadevan. However, in contrary to the previous findings; none of the

patients with severe envenomation in our study developed severe pain with the improvement in clinical state.<sup>1,4,5</sup>

#### Paresthesia

Paresthesia was present in 47 (44.34%) patients in this study, which persisted for 8 h to 2 days. Pulmonary edema and LVS3 were present in 18 patients each; ECG changes in the form of T wave and ST segment changes were present in 26 patients, suggesting significant association of paresthesia with cardio-pulmonary manifestations, but it was not statistically *significant* ( $p \ge 0.5$ ).

## Swelling at the site of sting

Swelling at the site was present in 42.5% of the patients. Three patients had local cellulitis and gangrene. 44% of patients with swelling had pulmonary edema ( $p \ge 0.5$ ) and 51% had ECG changes ( $p \ge 0.5$ ) as opposed to 33% and 47% without swelling respectively, which is statistically not significant which goes in par with previous studies. Hence, presence of local swelling does not appear to have any association with subsequent development of features of severe envenomation.

# Autonomic manifestations

Majority of signs and symptoms of scorpion sting envenomation are due to dysautonomia.

Table 5 compares the autonomic manifestations in different studies.

Most common sign was tachycardia which was present in 92 (86.8%) patients, more than that seen in previous

reports. This may be probably because of inclusion criteria (those with systemic manifestations only were included in the study).

Next common autonomic manifestation is profuse sweating, lasted for 8-10 h, which was noted in 72.6% of the patients, correlates with previous reports. All patients with pulmonary edema had profuse sweating except 2 patients, 50 of 52 who had ECG changes had profuse sweating indicating association of this finding with cardio-pulmonary manifestation ( $p \le 0.0001$ ).

Pulmonary edema was noted in 40 (37%) patients, which was slightly more than that observed in Mahadevan and Das series. <sup>1,2</sup> But much less than that seen by Bahloul et al. <sup>10</sup> and Bouaziz et al. <sup>11</sup>

Hypertension was noted in 46 (43.4%) patients, majority had moderate hypertension, only 5 patients had severe hypertension (180/100 mm of Hg and above). 31 patients became normotensive within 6 h, 12 patients in next 24 h, only 3 patients remained hypertensive after 24 h. All the patients were treated with prazosin irrespective of the blood pressure levels.<sup>2</sup>

Other manifestations like palpitations were noted in 20, dilated pupils in 25 and piloerection in 23 patients. 50% of these patients had pulmonary oedema and LVS3 gallop.

Most common parasympathetic manifestation is excessive salivation noted in 30 patients; more than half of the patients had pulmonary edema and LVS3. Next common is nausea and vomiting seen in 24.5% of the patients, in this group 61% had pulmonary edema, LVS3 and 58% had ECG changes. This is very significant association, suggesting that if these are present at presentation subsequent evolution to severe envenomation is very high.

Priapism; that is considered as cardiac premonitory sign in scorpion sting envenomation by Bawaskar and Bawaskar, was present in 14 patients in this study. <sup>12</sup> Not all the patients with priapism had cardio-pulmonary manifestations, only

50% (7) of the patients had pulmonary edema (p = 1) and LVS3 and ECG changes. None of the features of severe envenomations was significantly associated with priapism.

Hypotension was noted in 14.2% of the patients that were much less compared to the previous series, this may because of the age composition of the study population. 12 of 15 patients with hypotension had pulmonary edema. Two patients presented with severe hypotension died, one patient who initially presented with hypertension developed hypotension after 6 h and succumbed to death after 14 h of hospital stay. Presence of hypotension is a poor prognostic factor ( $p \le 0.0001$ ).

Miosis and dysphagia were present in 5 cases each.

## Other cardio-respiratory manifestations

Cold peripheries seen in 51 (48%) patients, which is less compared to RajaRajeswari et al. (68%) and Das (93.75%). This discrepancy may be because of inclusion of mainly pediatric population in their study group. <sup>1,8</sup> 36 (34%) patients had LVS3 among them 31 patients had pulmonary edema, and 4 had breathlessness without pulmonary edema. 12 patients had Grade 2-3/6 systolic murmur at the apex, two of them died and in remaining patients murmur disappeared after variable period. Extensive wheezes were present in 14 patients, probably due to bronchospasm and hemoptysis was present in 13 patients.

## Central nervous system manifestations

Altered sensorium was seen in 19 patients three of them died, two presented with hypotension and one with hypertension developed hypotension latter. Three patients developed the hemiparesis on the 3<sup>rd</sup> day of envenomation, computed tomography scan brain showed acute ischemic infarct in them. In many studies altered sensorium was attributed to hypertensive encephalopathy, other studies have hypothesized that hypertensive encephalopathy was not the only cause for altered sensorium.<sup>6,13</sup> In the present study out of 19 patients with altered sensorium only 5 were

			8				
Sympathetic	Number (%)						
abnormality	RajaRajeswari <sup>7</sup> (n=68)	Poonking <sup>6</sup> (n=45)	Mahadevan² (n=100)	Das <sup>1</sup> (n=32)	Present (n=106)		
Tachycardia	46 (68)	17 (38)	62 (62)	26 (81.26)	92 (86.8)		
Tachypnea	46 (68)	22 (49)	-	-	51 (48)		
Hypertension	-	-	-	-	46 (43.4)		
Pulmonary edema	2 (3)	-	22 (22)	3 (9.37)	40 (37)		
Profuse sweating	46 (68)	14 (31)	52 (52)	25 (78.12)	77 (72.6)		
Bra6dycardia	2 (3)	8 (18)	9 (9)	2 (6.25)	7 (6.6)		
Hypotension	46 (68)	9 (20)	56 (56)	13 (40.6)	15 (14.2)		
Salivation	-	45 (199)	-	-	30 (28.3)		
Nausea/vomiting	29 (40)	42 (93)	-	-	26 (24.5)		

Table 5: Some of the autonomic findings in different studies.

hypertensive, 5 patients had hypotension, 3 had cerebral infarcts. Hence, the hypertensive encephalopathy is unlikely to be the sole cause of altered sensorium. Other causes could be hypoxic encephalopathy, infarction, cerebral edema.<sup>6,13</sup>

#### Pain abdomen

Pain abdomen was present only in 11 (10.4%) cases in our study that is in contrast to the observation made by poonking wherein it was present in 71% of the cases. abdominal tenderness was present in only 7 (6.6%) crases as opposed to 62% of cases in poonkings series.<sup>6</sup> this may be because variation in the species and venom composition.<sup>4,5,14</sup>

All the patients were treated symptomatically with supportive care as detailed in the methodology. Several studies have been published both far and against the use of antivenom. However, we could not use the antivenom as it was not available at our institution.

Scorpion envenomation is frequently associated with autonomic storm, which can be lethal if not identified early. Presence of profuse sweating, nausea/vomiting, hypotension, pulmonary edema and ECG changes at presentation are associated with poor prognosis.

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