

## ORIGINAL ARTICLE

# PREDICTORS OF IN-HOSPITAL MORTALITY IN PATIENTS WITH SNAKE BITE IN POPULATION OF KARACHI, PAKISTAN

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## ABSTRACT

**Background:** Snake bite remains major public health problems worldwide. The objective of this study was to determine predictors of in-hospital mortality in patients presenting with snake bite in population of Karachi, Pakistan.

**Materials & Methods:** It was cross-sectional study conducted at Department of General Medicine, Postgraduate Medical Center, Karachi, Pakistan from 11th June 2016 to 10th August 2017. 300 patients with snake bite were selected. Age, gender, acute kidney injury, vomiting and in-hospital mortality were variables. Except age, all variables were nominal and were analyzed by frequency and percentage. Cox-proportional-hazard regression model was applied and hazard ratios were calculated along with 95% confidence intervals (CI) to assess the strength of association between predictors i.e. age, gender, AKI and vomiting and outcome (in-hospital mortality). Kaplan-Meier and time to event plot were used to investigate all patients who were on follow-up for 7 days from admission. Log-rank test was used to identify the predictors of in-hospital mortality for significant independent influence on prognosis at alpha .05.

**Results:** The mean age of the sample was  $27.7 \pm 14.58$  years. Out of a sample of 300 patients, 221 (73.7%) were males and 79 (26.3%) females. The frequency (%) of AKI was 102 (66%), vomiting 122 (40.7%) and of in-hospital mortality 31 (10.3%). The probability of survival at day 7 was 81.8%. Vomiting [hazard ratio 6.86 (95% CI: 2.78-16.93),  $p < 0.001$ ] and acute kidney injury [hazard ratio 3.85 (95% CI: 1.75-8.45),  $p < 0.001$ ] were associated with higher risk of death in adjusted analysis.

**Conclusion:** Acute kidney injury and vomiting are strong predictors of mortality among patients with snake bite. These predictors can be helpful for clinicians in assessing prognosis of their patients more accurately and by early management of these factors, mortality & morbidity can be reduced.

**KEY WORDS:** Snake Bites; Acute Kidney Injury; Mortality; Vomiting; Risk factors; Survival; Antivenoms; Poisoning.

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## INTRODUCTION

There are more than 3000 species of snakes in the world; out of which some 600 are venomous and over 200 are considered to be medically important.<sup>1</sup>

Snake bite (SB) is a global public health problem, more common in tropical and subtropical regions. Annually some 5.4 million snake bite cases are re-

ported globally, resulting in 1.8 to 2.7 million instances of envenoming (poisoning). Likewise annually 81,410 to 137,880 deaths are reported with three times as many amputations and other permanent impairments. Majority of SB cases are reported from Asia, Africa and Latin America. Annual data from Asia shows about two million envenomings and from Africa there are 435,000 to 580,000 instances of snake bite requiring treatment.<sup>2</sup>

SB is a major issue in middle and low income rural areas, impacting farmers, children and women in particular. The highest prevalence was recorded in countries with minimal and poorest medical services.<sup>2,3</sup> Very few countries provide accurate epidemiological statistics of the SB in their countries. Most of the information accessible is focused on hospital reports, which show a relatively low number

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of SB incidents.<sup>4,5</sup> Prevalence and incidence of SB vary due to many factors, such as the environment, biodiversity, ecology, distribution of the snakes and human densities in various geographical regions.<sup>6</sup>

Venomous snake bite are acute medical emergencies. These may cause severe paralysis which may prevent breathing, cause bleeding disorders that may be fatal, cause irreversible kidney damage and severe local tissue destruction leading to permanent disability and limb amputation. Most of these effects may be prevented or reversed by wide availability and timely administration of effective antivenoms.<sup>1</sup>

The odds of fatality due to SB can be reduced and prevented, if the patient is treated without wasting too much time.<sup>7-10</sup> A Malaysian study showed that most of the SB cases are of nonvenomous, but venomous bites are the source of significant injuries and deaths.<sup>11</sup> In India about 5.4 per 100,000 individuals mortalities occurred yearly due to SB whereas in Burma, SB is the 5<sup>th</sup> most frequent cause of fatality with estimated ratio of 3.3 per 100,000 individuals.<sup>12</sup> According to a Pakistani survey, the estimated fatality rate is 1.9 per 100,000 individuals due SB.<sup>12</sup>

The rationale of study was that the studies on the subject under consideration are scarce regarding our population (such as Karachi, Sindh) and secondly most of the studies are done on retrospective data. The objective of this study was to determine the predictors of in-hospital mortality in patients with snake bite in population of Karachi, Pakistan. So that strategies could be devised for resources allocation and for prompt management to decrease the morbidity and mortality.

## MATERIALS AND METHODS

**Design, Settings & Duration:** It was a cross-sectional study conducted at the Department of General Medicine, Postgraduate Medical Center, Karachi, Pakistan from 11<sup>th</sup> June 2016 to 10<sup>th</sup> August 2017. Approval from Ethical Review Committee of the hospital was sought prior to conduct of the study. Informed consent from the patients or their attendants was taken after the purpose, procedure, risks and benefits of the study were explained to them.

**Sample Size, Technique & Selection:** The sample size was calculated by using Open EPI online sample size calculator, based on frequency of in-hospital mortality in snake bite cases 11%<sup>13</sup>, margin of error as 3.6%,  $n=291 \approx 300$  patients with snake bite. Non-probability consecutive sampling technique was used. All patients with snake bite presenting within 12 hours of incident were eligible. Patients with documented histories for a pre-existent renal disease (serum creatinine of  $>1.5$  mg/dL), of bilateral small kidneys, diabetes mellitus, hypertension and exposure to toxins/nephrotoxic drugs, obstructive nephropathy, loss

of the corticomedullary differentiation or other renal pathologies were excluded from the study.

**Conduct of Procedure:** All these patients were admitted. Researcher took brief history for duration of snake bite and demographics. For AKI baseline investigations including creatinine were sent to the laboratory at the time of admission. Serum creatinine level was repeated after 48 hours and increase in the serum creatinine concentration of  $\geq 0.3$  mg/dL within 48 hours from the baseline value was taken as AKI.

**Data Collection & Analysis Plan:** Age in years and gender were two demographic variables. Acute kidney injury (AKI) and vomiting were two research variables taken as predictors and in-hospital mortality was outcome variable (variable of interest). Death within seven days of admission was labeled as in-hospital mortality.

Descriptively numeric variable such as age was analyzed by mean and standard deviation. Nominal variables such as gender, AKI, vomiting and mortality were analyzed by frequency and percentage.

Cox-proportional-hazard regression model was applied and hazard ratios were calculated along with 95% confidence intervals (CI) to assess the strength of association between predictors i.e. age, gender, AKI and vomiting and outcome (in-hospital mortality). Kaplan-Meier and time to event plot were used to investigate all patients who were on follow-up for 7 days from admission. Log-rank test was used to identify the predictors of in-hospital mortality for significant independent influence on prognosis. P-value  $\leq 0.05$  was taken as statistically significant. All the data were analyzed through IBM SPSS Statistics for Windows, v.23.0 (IBM Corp., Armonk, NY).

## RESULTS

The mean age of the sample was  $27.7 \pm 14.58$  years. Out of a sample of 300 patients, 221 (73.7%) were males and 79 (26.3%) females. The frequency (%) of AKI was 102 (66%) and of vomiting was 122 (40.7%). The frequency of in-hospital mortality was 31 (10.3%).

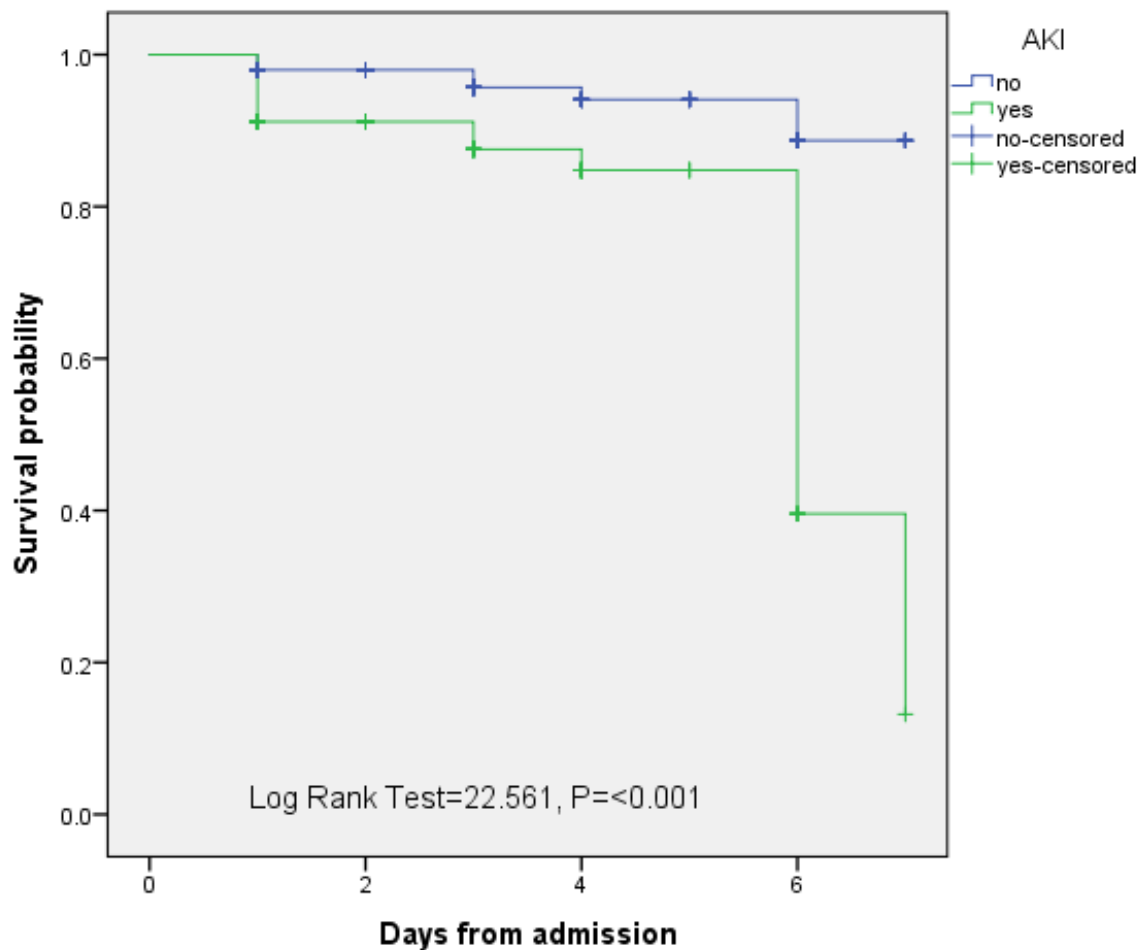
In univariate analysis only risk factors i.e. AKI & vomiting were significantly associated with mortality. In the final model, AKI [HR: 3.85 (95% CI: 1.75-8.45)] and vomiting [HR: 6.86 (95% CI: 2.78-16.93)] were independent risk factors for in-hospital mortality. (Table 1)

Compared to those who did not had AKI, patients with AKI had 3.85 (95% CI 1.75-8.45) times more chances of death within 7 days ( $P = <0.001$ ). (Fig. 1)

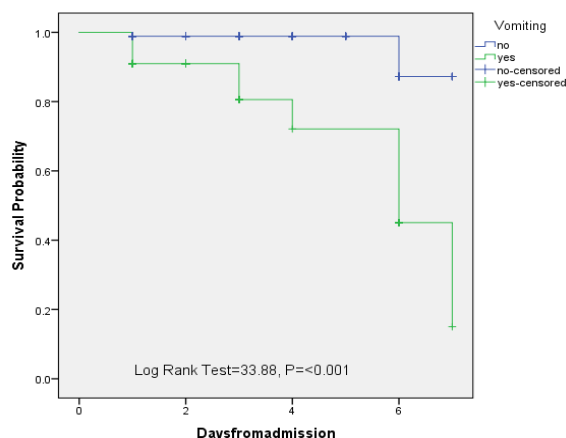
The Kaplan-Meier analysis identified patients who vomited after snake bite were 6.86 times more likely to die during the 7 days study period than those who didn't vomit ( $P = 0.001$ ). (Fig. 2)

**Table 1: Predictors of in-hospital mortality in patients presenting with snake bite in population of Karachi, Pakistan (n=300)**

Factors		Sample size (%)	Mortality 31 (10.3%)	Univariate analysis		Multivariate analysis	
				Unadjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Age in years		27.7±14.58	--	0.99 (0.96-1.01)	0.39	--	--
Gender	Male	221 (73.7)	24 (8.00%)	Reference	0.296	--	--
	Female	79 (36.3)	7 (2.33%)	5.05 (2.32-10.9)			
AKI	Absent	198 (34.0)	9 (3.00%)	Reference	0.001	Reference	0.001
	Present	102 (66.0)	22 (7.33%)	8.52 (3.47-20.91)		3.85 (1.75-8.45)	
Vomi-ting	Absent	178 (59.3)	6 (2.00%)	Reference	0.001	Reference	0.001
	Present	122 (40.7)	25 (8.33%)	8.52 (3.47-20.91)		6.86 (2.78-16.93)	



**Figure 1: Kaplan-Meier survival probability estimates for time from hospital admission to mortality in patients with snake bite in population of Karachi, Pakistan with respect to AKI (n=300)**



**Figure 2: Kaplan-Meier survival probability estimates for time from hospital admission to mortality in patients with snake bite in population of Karachi, Pakistan with respect to vomiting (n=300)**

## DISCUSSION

Mean age for patients in our sample was  $27 \pm 14.58$  years and most of the patients were males. A greater percentage of males in our sample can be due to the fact that males normally go to the fields every day, are more busy at night, move more frequently, while females often remain in and around compounds and homes. In a study by Kulkarni, et al. 68% of the victims were male and 32% were female.<sup>14</sup> In another study by Bawaskar, et al. higher percentage of male victims was reported as compared to female (63% vs 37%).<sup>15</sup>

In the present study we observed that 66% (102/300) of the Snake bite (SB) victims developed acute kidney injury (AKI). In India studies showed that up to 32% of the SB victims developed AKI.<sup>8,16</sup> In study by Patil, et al. 21% of SB patients developed AKI, whereas in a study by Ali, et al. 17% of the SB victims developed AKI.<sup>17,18</sup> Hence these proportions are lower than our study findings. A number of authors have studied AKI in SB, its association with various coagulation disorders and following fatalities in those patients. In present study we found that AKI was the potential and independent predictor of in-hospital mortality.

We also found that vomiting was present in 40.7% (122/300) patients. In-hospital mortality was 8.33% (25/300) in those with vomiting and 2.00% (6/300) in those without vomiting. Vomiting is also an independent risk factor for mortality in the present study ( $p < 0.001$ ). This is in agreement with the findings of Kalantri, et al. who also concluded that vomiting was the significant predictor of mortality among patients with SB.<sup>13</sup>

In study by Athappan, et al. the mortality rate was found as 22.6% in patients with SB.<sup>19</sup> In 336 cases

studied by Kularatne, the mortality was present in 9 cases only (2.6%).<sup>20</sup> In the 633 cases studied by Kulkarni, et al. the mortality rate was 5.2% (33 cases).<sup>14</sup> In a study conducted at a rural hospital of India by Kalantri, et al. found that 11% in-hospital mortality occurred in patients with venomous snake bite, however the survival probability was noted as 83% at day 7 from admission.<sup>13</sup> Thus, mortality rate described in various studies varies from 2.5% to 25%. The data of our study revealed that 10.3% patients died with snake bite and survival probability at 7 days was 81.8%.

## CONCLUSION

We found that acute kidney injury and vomiting are strong predictors of mortality among patients with snake bite. As large population lives in rural areas of Pakistan, so they are more at risk of snake bite. These predictors can be helpful for clinicians in assessing prognosis of their patients more accurately and also useful for decision-making and by early management of these factors, rate of mortality & morbidity can be reduced.

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**CONFLICT OF INTEREST**

Authors declare no conflict of interest.  
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None declared.

**AUTHORS' CONTRIBUTION**

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	HK, AB
Acquisition, Analysis or Interpretation of Data:	HK, AB, KA, NNB
Manuscript Writing & Approval:	HK, AB, KA, NNB

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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