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Systematic Review

Profile of Snake Bite Induced Acute Kidney Injury in Indian Population: A Systematic Review

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Abstract

Snakebite deaths and disability is a major public health challenge in India. India has more than 300 species of snakes, of which 60 are labelled venomous or mildly venomous. India has the highest number of deaths because of snakebites in the world. Data regarding the actual number of SAKI and requiring HD and their complications are inadequate in our country**.** This study aimed to study the profile of snake bite induced acute kidney injury in Indian population. A systematic search was conducted to identify papers published in PubMed, Google Scholar and Cochrane electronic databases from January 2017 to March 2022 with the PRISMA statement. Totally, 1377 were listed in our review. After removing duplicates, not accessible, incomplete, subscription articles only 13 studies were found eligible for the present systematic review. The study findings indicate that the most common snake causing acute kidney injury is viper. Mortality is less in patients underwent early hemodialysis.

Keywords: Snakebite, Acute kidney injury, India.

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Introduction

Snakebite deaths and disability remain a major public health challenge also for poor rural communities in many parts of Asia, Africa, Latin America and Oceania. The World Health Organization (WHO) estimates that 81,000–138,000 people die each year from snakebites worldwide, and about three times that number survive and but are left with amputations and permanent disabilities (World Health Organization (WHO), 2019a). Snakebite was re-designated as a neglected tropical disease (NTD) in 2017, which was removed from the list in 2013, re-considering the problem of snakebite in developing and tropical countries, which contributes 95 per cent of the total snakebites of the world, it was re-designated as a Category A of the NTD by the WHO10 with the hope that this declaration would provide an ample opportunity to attract investment and research funding for further improvement of snakebite management in developing countries.[1] A recent study estimates the

total number of snakebites to range from 1.11 to 1.77 million in 2015 and 1.2 million snakebite deaths (average 58,000/year) from 2000 to 2019 in India.[1] India has more than 300 species of snakes, of which 60 are labelled venomous or mildly venomous. Majority of snakebites in India, result from 4 species namely Daboia russelii (Russell's viper), Naja naja (common Indian Cobra), Bungarus caeruleus (common krait) and Echis carinatus (saw-scaled viper) and these are not uniformly distributed through the length and breadth of the country.[2]

AKI is now defined by the RIFLE criteria (risk, injury, failure, loss, end-stage kidney disease) and is not just ARF. It incorporates the entire spectrum of the syndrome, from minor changes in renal function to the requirement for renal replacement therapy [3]. The exact pathogenesis of AKI following snakebite is not well established because of the lack of a reproducible animal model. However, a number of factors may contribute, including bleeding, hypotension, circulatory collapse, intravascular hemolysis, DIC, microangiopathic hemolytic anemia, and also the direct nephrotoxicity of the venom. Bleeding either into tissues or externally and loss of plasma into the bitten extremity can produce hypotension and circulatory collapse. These effects are caused by venom metalloproteinases that degrade basement membrane proteins surrounding the vessel wall, leading to loss of integrity.[4] Hemorrhagic toxins have been isolated from the venom of many snakes of the Viperidae and Crotalidae families.[5] In addition, vasodilation and increased capillary permeability can aggravate the circulatory disturbances of shock. Hemolysis results from the action of phospholipase A2, which is present in almost all snake venoms. Phospholipase A 2 causes hemolysis directly by hydrolysis of red blood cell membrane phospholipids or indirectly via production of the strongly hemolytic lysolecithin from plasma lecithin. The human hemostatic system is regulated through a number of critical interactions involving blood proteins, platelets, endothelial cells, and subendothelial structures. Snake venoms, particularly those from the viper and pit viper families, contain many proteins that interact with members of the coagulation cascade and the fibrinolytic pathway. Whatever the predisposing factor or ultimate renal lesion, it is the interplay of chemical, and immune mediators produce in different pathway responsible for kidney injury.[4]

In Some studies, Pathological investigations of human fatal cases revealed renal cortical necrosis, distal nephron nephrosis, thrombotic microangiopathy, and acute tubular necrosis.[6]

Majority of studies reported either acute tubular or cortical necrosis found on renal histological examination. Glomerular changes have been described in rare cases, but their significance is not known.[4] An incidence of renal involvement with snakebite envenomation of 1.4–28% has been reported in various series,[7] and incidence of ARF is 10–32%. [8-10] On the Indian subcontinent, AKI develops after bites by snakes of the viper family such as Russell's viper, the saw-scaled viper (Echis carinatus), and pit vipers. The incidence of AKI varies from 13% to 32% in India after Russell's viper or E.carinatus bites[11-13].

Materials and Methods

Search strategies

A systematic search from January 2017 to March 2022 on Google Scholar, PubMed, and Cochrane electronic databases was carried out. The Guidelines used for this systematic review were from the preferred reporting items for systematic reviews and meta-analyses (PRISMA). The search was conducted by two reviewers who independently screened the databases through the following terms: "snakebite" AND "acute kidney injury" AND "India". Any discrepancies were resolved by consensus with a third reviewer. Studies

published in English language were included. Only open access journals and articles with full free text were included.

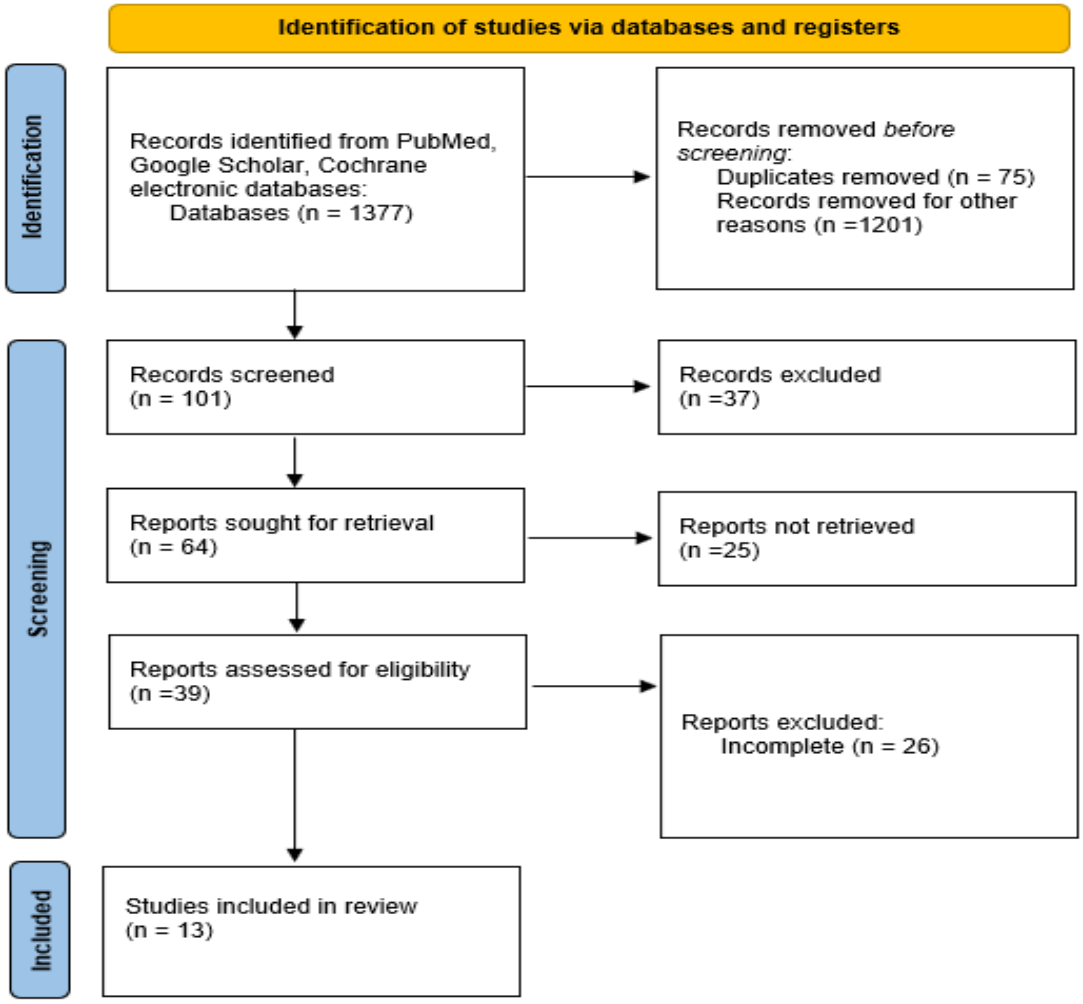

Figure 1: PRISMA flow diagram showing a search strategy, identification and selection of articles for review

Inclusion criteria

A. Studies done in India and published in national and international journals.
B. Studies about snakebite and Acute kidney injury.
C. Only published studies.

The following articles are included in the study (1) Retrospective studies (2) Prospective observational studies.

Exclusion criteria

Articles were excluded if the following standards were encountered: (1) Duplicate publications, (2) Studies done outside India. (3) Studies done for other complications of snake bite.

Data extraction

The following details were extracted for each of the included studies: the first author's name, publication date, type of study, the study location, duration of study, sample size, requirement of Hemodialysis and Death. (Table.1)

Data synthesis and Analysis

The data was analyzed and categorized in to prospective and retrospective studies. Further data was analyzed based on studies about total snake bite cases and percentage of aki cases. Data was analyzed for the requirement of Hemodialysis in aki cases in the studies done only on aki cases. we used Microsoft Office Word, Excel, and p value calculated with https://www.socscistatistics.com.

Results

In our review the percentage of patients developing aki following snake bite was 23.5% (Table.2). This is corelated with previous studies [11-13]. The percentage of patients underwent hemodialysis (Table.3) were 39.72%. The percentage of Deaths (Table.4) in AKI patients was 7.78%. There was a statistically significant difference ($p < 0.05$) between the retrospective and prospective studies in the incidence of aki.

Table 1:

Author	PMCID	Type of study	Place of study	State	Duration of study	Total snake bite cases	Total AKI cases	HD	Death
Sanjay Vikrant [14]	28540205	A retrospective study	Indira Gandhi Medical College Hospital	Himachal pradesh	July 2003 to June 2016		121	99	11
Ramulu Pulimaddi [15]	29664034	prospective	Osmania General Hospital	Telangana	November 2013 to July 2015		100	12	6
Abhishek KB [16]		prospective	Department of Emergency Medicine at M S Rammaih Medical	Karnataka	August 2017 to September 2018		100	60	14
P.S. Priyamvada [17]		prospective	Jawaharlal Institute of Post Graduate Medical Education and Research,	Puducherry	January 2016 to June 2017		184	114	35
Tarun K George [18]	31823930	retrospective	Christian Medical College (CMC) vellore,Pondicherry Institute of Medical Sciences (PIMS)	Tamilnadu, Puducherry	January 2005 to December 2015.	866	184	70	11
Rupal Padhiyar [19]	30341870	prospective	Lokmanya Tilak Municipal Medical College, Mumbai	Maharashtra	2015	64	8	4	
Kripasindhu Gantait [20]	31823932	prospective	Midnapore Medical College	West Bengal	January 2012 to December 2015	1220	660	180	28
Viney Sambyal [21]		retrospective	Government Medical College, Jammu,	Jammu and Kashmir	January 2016 to December 2016	100	7	-	-
Sameer Anand [22]		prospective	GMC Jammu	Jammu and Kashmir	November 2016 to October 2017	300	62	-	-
Dr.Hanuman Ram Choudhary [23]		prospective	Government Medical College, Barmer,	Rajasthan		50	15	-	-
Arjimand Yaqoob [24]		retrospective and prospective study	Sher-i-kashmir Institute Of	Jammu and Kashmir		108	5	-	-
Rituparna Ghosh [25]		retrospective	Midnapore Medical College	West Bengal	January 2012 to December 2016	6343	1268	-	-
Kaushik Mana [26]		prospective	Midnapore Medical College	West Bengal	1 January 2013 through 31 December 2016	1160	171	-	-

Table 2: Showing Percentage of AKI patients in Total snake bite cases

Type of Study	Total snake bite cases	No of AKI patients	Percentage
Retrospective	7309	1459	19.96%
Prospective	2794	916	32.78%
Total:	**10103**	**2375**	**23.51%**

Table 3: Showing Percentage of Hemodialysis (HD) done

Type of Study	No of AKI patients	HD	Percentage
Retrospective	305	169	55.40 %
Prospective	1052	370	35.17 %
Total:	**1357**	**539**	**39.72 %**

Table 4: Showing Percentage of Deaths in No of AKI patients

Type of Study	No of AKI patients	Death	Percentage
Retrospective	305	22	7.21 %
Prospective	1044	83	7.95 %
Total:	**1349**	**105**	**7.78 %**

Table 5: Showing Aki and non-Aki cases

Type of Study	No of AKI patients	Non-AKI	Total
Prospective	916	1878	2794
Retrospective	1459	5850	7309
Total:	**2375**	**7728**	**10103**

The chi-square statistic is 184.8302. The *p*-value is < 0.00001. Significant at $p < .05$.
The chi-square statistic with Yates correction is 184.1178. The *p*-value is < 0.00001. Significant at $p < .05$.
This systematic review demonstrates that snake bite leading to acute kidney injury was a common condition in all over India even though the distribution of snakes differs along the length and breadth of our country. The most common snake leading to aki was viper. Majority of the patients recovered without the need for hemodialysis. In those requiring HD mortality was less. studies are prospective and retrospective or both, did not use a sample size calculation, were single center and were underpowered. Only one study was conducted at two centers. retrospective studies suffered with lack of proper data. There is an urgent need for standardization in the way that aki patients are assessed. Renal injury can result from envenoming by a range of snake species. Outcome measures in these studies have focused on acute renal injury; based on levels of serum creatinine and oliguria. Internationally recognized criteria for the diagnosis of acute kidney injury are available, and these were adopted in two of the included studies. Although the need for Hemodialysis / renal replacement therapy (RRT) is crucial in the management of AKI, there is wide variation about the optimal timing for initiating and stopping this in acute kidney injury

Conclusions

Acute kidney injury following snake bite is common in entire india even though the distribution of snakes differs along the length and breadth of the country. Viper bites is the most common cause of aki in this study. Majority of the patients recovered without the need for hemodialysis.

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