White Paper

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White paper on venomous snakebite in India

Joy Kumar Chakma[1], Jaideep C. Menon[2], R.S. Dhaliwal[1] & Indian Council of Medical Research[#]

[1]Division of Non-Communicable Diseases, Indian Council of Medical Research, New Delhi & [2]Department of Preventive Cardiology, Amrita Institute of Medical Sciences, Amrita University, Kochi, Kerala, India

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Venomous snakebite is one of the leading preventable causes of mortality and morbidity with tremendous socio-economic impact on the family and nation. Venomous snakebite has been relisted as a neglected tropical disease after having been removed off the list in 2013. This paper discusses the various reasons which could be attributed to the high mortality and morbidity due to venomous snakes and also provides recommendations on policy decisions, improvement on the quality of venom and anti-snake venom and in promoting awareness on how to avoid snakebite.

Key words Anti-snake venom - neglected tropical disease - snakebite - venomous

[#]ICMR-National Task Force for Research on Snakebite:

Chairman: S.K. Maulik, Professor, Department of Pharmacology, AIIMS, New Delhi

Members (in alphabetical order): Ajay Kumar Tahlan, Central Research Institute, Kasauli; Ashish Mukherjee, Professor, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur; B. S. Vishwanath, Professor and Chairman, Department of Biochemistry, University of Mysore, Mysuru; Gaurav Gupta, National Professional Officer (Injury and Disability Prevention), WHO India Office, New Delhi; Gowri N. Sengupta, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; Jaideep C. Menon, Amrita Institute of Medical Sciences, Kochi; Jose Louise, Founder, Indiansnakes.org, Wildlife Trust of India, Noida, Uttar Pradesh; Karthik Sunagar, Centre for Ecological Sciences, Indian Institute of Science, Bengaluru; Kulbhusan Tikoo, National Institute of Pharmaceutical Education and Research, Mohali; Nishigandha Naik, Director, Haffkine Institute for Training and Research, Mumbai; Praveen Aggarwal, All India Institute of Medical Sciences, New Delhi; Romulus Whitaker, Global Snakebite Initiative, Centre for Herpetology/Madras Crocodile Bank, Chennai; R.S. Dhaliwal, Indian Council of Medical Research, New Delhi; Sanjeev Kumar, Ministry of Health and Family Welfare, Government of India; Siddharth Daga, Vins Bioproducts Limited, Hyderabad; Shrimati Shetty, ICMR-National Institute of Immuno-haematology, Mumbai; Vijay Chaudhary, Centre for Innovation in Infectious Disease Research, Education and Training, Delhi University, South Campus, Delhi, India.

Venomous snakebite is a significant cause of morbidity and mortality in India, as also in other parts of South-East Asia and sub-Saharan Africa, especially in the rural hinterlands where medical facilities are lacking[1]. Snakebite is most often an occupational, domestic or environmental hazard affecting mostly males between 20 and 55 yr of age[1-3]. The socio-economic fallout of this is immense, in the case of death of the only earning male member of the house as is not uncommon[4]. The estimated number of snakebites worldwide has been put as 5.4 million, resulting in 2.5 million envenomation and 81,000–138,000 deaths, annually[5-7]. It is estimated that there are over 1,000,000 snakebites in India alone causing 58,000 deaths annually and significant disability in almost four times the number[5,7,8]. The National Health Profile 2019 data on snakebites reported 164,031 snakebite cases and 885 deaths in 2018[9]. Thus, there is a discrepancy between WHO estimates and the reported figures, making it all the more logical to comprehensively study the incidence and deaths due to snakebite.

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 WHO[10] 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. One of the major reasons cited for snakebite being removed off the NTD list was that there were not enough data from developing countries like India[10].

The Big 4 and other venomous species

India has more than 300 species of snakes, of which 60 are labelled venomous or mildly venomous. Majority of snakebites in India, result from what are dubbed the Big 4 species namely *Daboia russelii* (Russell's viper), *Naja naja* (common Indian Cobra), *Bungarus caeruleus* (common krait) and *Echis carinatus* (saw-scaled viper). All the Big 4 are not uniformly distributed through the length and breadth of the country with distribution dependent on multiple factors, not limited to rainfall, altitude, habitat and availability of prey[11]. Importantly, there are also certain species which are specific to certain geographical areas and whose venom is not neutralized by the available polyvalent anti-snake venom (ASV). These include the *Naja kaouthia, Bungarus fasciatus, Bungarus niger, Bungarus sindanus, Trimeresurus* species*, Hypnale hypnale, Echis carinatus sochureki, Ovophis monticola* and *Ophiophagus hannah*. In certain parts of our country, bites from the above-mentioned species are more common than that of the Big 4 species[12-16]. It was believed that the available polyvalent ASV would help neutralize venom fractions of the above-listed snakes through cross-reactivity, with fractions neutralizing venom of the Big 4. There are no data till date to support this belief, and neutralization studies done *in vitro* using venom from the non-Big 4 snakes suggest poor degree of neutralization with the available polyvalent ASV[17]. This also could be the reason behind the extravagant doses of ASV required in certain parts of north and east India, much higher than the usual standard of 20 vials[18,19].

Equally important is the fact that venoms of the same species have shown significant differences in composition and biochemical and toxic profiles when studied from different zones of India. It is known that the available polyvalent ASV acts best in snakebites from the southern and western parts of India and not as well in the northern and eastern parts of the country. This has been proven from *in vitro* binding studies as well as animal studies and could again be a reason for the exceedingly high doses of ASV needed for neutralization in northern and eastern parts of India[18,19].

The only scientifically validated treatment for venomous snakebite is ASV. The ASV available in India is polyvalent and neutralizes the venom of the Big 4 species. Each millilitre of ASV as per the label neutralizes 0.6 mg of *D. russelii* and *N. naja* venoms and 0.45 mg venom of *B. caeruleus* and *E. carinatus*[20]. Each vial contains 10 ml of ASV which in effect should neutralize ten times the above-mentioned amounts of venom. The average ASV required is about 20 vials for a victim[20].

Polyvalent ASV continues to be manufactured by a process, first established by the Frenchman Albert Calmette[21], which has not changed much over the past 100 odd years. The ASV is constituted of $F(ab')^2$ fraction from pepsin digestion of IgG. The advantage of $F(ab')^2$ lies in that cleaving off the Fc fraction from the IgG makes adverse reactions less likely. The rate of adverse reactions, usually mild, to the available ASV is about 27-31 per cent according to most studies in India[2,3]. The quality of the ASV depends on

the quality of the venom used for raising antibodies in horses and finally on the quality of the antibodies raised in horses.

Venom

The Irula Snake Catchers' Industrial Cooperative Society, Chennai[22], is the major supplier of venom for the whole country both for research purposes and for inoculation into equines for raising antibodies. The Irulas catch the Big 4 species from the wild; milk them at weekly intervals (maximum of 4 milkings) for a period of up to a month and release the snakes back into the wild, preferably from the same location that they were caught from, after tagging them. The venom is ideally lyophilized (freeze dried), immediately stored and sold as per the applicable governmental rules. The Irulas have a permit to milk up to 8000 snakes a year from the Big 4 species. Ideally, the venom samples used for ASV production should be checked for quality and salivary contamination[22].

The practice of using venom from a single source in south India to manufacture ASV for the whole country contradicts accumulated scientific evidence which suggests that venom of the same species from different geographical locations in the country has different physico-biochemical constituents and thereby toxicity profiles[17]. Studies have shown that there are significant differences in enzymatic and non-enzymatic protein constituents between venom sourced from the four zones of India, North, South, East and West, as also their neutralization by the available ASV[17,18]. The available ASV best neutralizes venom fractions from snakes from the southern and western parts of India and not as well from venom from the northern and eastern parts. *In vitro* studies, biochemical as well as proteomic analyses, have indicated geographical variation in venom composition in the same species of snake[19,20]. These differences result in the commercial ASV prepared against the venom samples from a particular geographical location of the country showing poor immune cross-neutralization and toxicity neutralization of the venom sample from the same species of snake but from other regions of the country[17,20]. Most of the commercial ASV-manufacturing companies use snake venom from southern parts of India, which has raised a serious concern over their efficacy in neutralizing the venom samples from other regions of India[20]. Further, species-specific differences in venom composition, for example between *N. naja* and *N. kaouthia*, have also been demonstrated, and this also results in partial immune-recognition and neutralization of *N. kaouthia* venom by *N. naja* antivenom[17,23-25].

Anti-snake venom (ASV)

The WHO made it mandatory to follow the prescribed good manufacturing practices (GMP) 2017 guidelines for the manufacturing of ASV[26]. The animals used for raising antibodies include horses, mules and donkeys. Animals have to be at least five years of age and can be bled for nine months a year with a mandatory three-month rest period. Ponies can be bled till the age of 18 yr, horses 22 and mules till the age of 25 yr. The maximum amount of blood that can be drawn as per Indian guidelines[27] is 1.5 per cent of body weight or 10 per cent of plasma volume of the equine. There are mandatory blood tests and screening to be done prior to bleeding with compulsory vaccination against certain diseases. It is also mandatory that the manufacturers continue to keep the horse in their facility even after they are no longer used for antibody production. The median effective dose of the batches of ASV is ascertained through in-house neutralization studies where pre-mixed cocktails of venom and ASV are injected into mice. The quality of the ASV depends on the health and hygiene of the equines used for antibody production. For the harvested antibodies to be effective as ASV, these should be snake venom-specific antibodies and not antibodies that the equine carries otherwise. The usual methods used for purification of antibodies are either with ammonium sulphate or with caprylic acid[26]. The lyophilized ASV is prepared from the serum, with the red blood cells being transfused back into the equine. As mentioned earlier, the health and fitness of the equine, inoculation methods and purification process are of prime importance in ensuring the quality of the finished product the ASV.

Snakes are the protected species as per the Schedule 11 of the Wildlife Act 1972[27]. Capturing, killing or milking any of the venomous species is an offence. This Act when passed in 1972 was instrumental in putting an end to a thriving snake skin industry, resulting in the wanton killing of thousands of snakes annually[27]. The flip side is that venom is now greatly protected and a hard-to-get commodity for research and for ASV manufacturing. There are only a few institutes with the necessary permission to milk venom on a commercial scale. What is available commercially comes at a prohibitive cost with an erratic supply in the necessary quantities of the Big 4 venom. The venom of the common krait and saw-scaled viper is difficult to procure in the

quantities required by the ASV manufacturers, which limits their capacity to produce polyvalent ASV. The captive breeding of snakes for venom collection is not followed in India, which is a common practice in other tropical countries[26]. If this technique is implemented in India, this would considerably lessen the number of snakes handled and relocated (snake relocation is thought to lead to the death of the snake in >50% of cases within a short period of time). This would also help in milking healthier snakes than in the wild, thereby improving the quality of the venom.

The treatment aspects

Most of the fatalities occur due to the delay in reaching hospital in time, which are preventable. The primary health centres (PHCs) would be the first interphase where the victim comes in contact with the health system. Many PHCs in the country lack the trained human resources and health facilities to admit and treat patients with snakebite. This compels the victims to go to alternate forms of treatment which are rampant in most parts of India (Kaviraj, Oza, Mantrik and Sarpa chikitsa)[2,3,13,14]. Doctors at the community- and taluk-level hospitals are sceptical in infusing ASV, fearing adverse reactions. Moreover, all doctors, may not be well versed with life support skills which become critical in areas where elapid (neurotoxic) bites are common[3,13,14]. There is no time in hand and a number of victims die in transit from the peripheral hospital to the referral hospital. Airway management is critical in elapid bites, and referral of patients should be after airway management[3].

Given the fact that India lacks a commercially available snake venom detection kit (SVDK), clinicians depend on the 'syndromic approach' for the diagnosis of envenomation. The syndromic approach involves observing for signs and symptoms along with blood tests, of which the whole blood clotting test is most commonly employed to diagnose viperidae bites, to decide as to whether there has been envenomation. It is only after envenomation is ascertained that ASV is infused[28]. Although there are protocols for the management of venomous snakebite including the one of the Ministry of Health and Family Welfare, Government of India[29], but the same has not been implemented uniformly in all treating hospitals, and snakebite continues to be treated according to the treating physician's discretion[2,3].

Given the magnitude of the problem of snakebite, it is mandatory that snakebite management be a part of either the mainstream internal medicine text or be included in the text of emergency medicine. Currently, 'venomous snakebite' is covered as a part of forensic medicine in most curricula. In addition, simple measures on preventing snakebite could be included in the curriculum of preventive and community medicine texts. Other hindrances in planning for the mitigation of venomous snakebite in India are the unavailability of data on incidence, morbidity, mortality, socio-economic burden, treatment patterns, *etc*. Most of the data available are hospital based (estimated that only 20-30% of victims actually present to hospitals)[13] and are thereby skewed[3]. The one Million Death study[7] estimated 45,900 annual deaths due to snakebite in 2005 in India, whereas according to the Ministry of Health & Family welfare, statistic, the number of deaths due to venomous snakebite in 2016 was 1300[9] deaths. A recent publication on the trends in snakebite-related mortality from a nationally representative mortality study suggests the estimates of death due to venomous snakebite in India in the 20-yr period 2000-2019 as 58,000/year[8].

Road map towards mitigation of the problem of venomous snakebite

Venom related

(*i*) Setting up zonal banks or venom collection centres preferably in five zones in India for ASV manufacturing or to use a pooled venom samples, representative of all regions, to immunize the equine. The resulting antivenom will cover regional differences in venom immunogenicity.

(*ii*) Including region-specific venoms for ASV manufacturing, for example – *N. kaouthia* in the ASV for the East and North-East, *H. hypnale* for Kerala and *E. sochureki* for Rajasthan.

(*iii*) Capacity building on breeding snakes in captivity so as to do away with milking from wild snakes.

(*iv*) Venom testing for purity and toxicity prior to equine inoculation.

(*v*) Ensuring supply of venom at reasonable rates both for commercial manufacturing of ASV and also for clinical research purposes.

(*vi*) Setting up a national venom research centre with facilities for biochemical, proteomic, genomic, taxonomic and toxicological studies of different snake species and venoms of India.

Anti-snake venom (ASV) related

(*i*) Region-specific ASV incorporating regional venoms of the Big 4 and other venomous species of that area/zone.

(*ii*) Caprylic acid/ammonium sulphate-based purification of venom.

(*iii*) Chromatographic run of ASV to remove non-essential antibodies.

(*iv*) To include ASV in the National List of Essential Medicines.

(*v*) Government institutes to check for the efficacy of all batches of ASV manufactured.

(*vi*) ASV is a scarce resource and should be used with due prudence; stocking ASV in all PHCs is no answer as what happens is referral of the case to the higher centre after infusion of 1 or 2 vials in all snakebites (including dry and non-venomous). ASV to be stocked in the public hospitals as per its usage.

(*vii*) Adjuncts to ASV using newer techniques of ASV manufacturing including phage display based *etc*. to be charted, and sources other than equine including chicken egg to produce IgY (yolk) antibodies, sheep and camels to be studied as options.

(*viii*) Monovalent antibodies to be developed.

(*ix*) Other venomous species specific to certain areas to have ASV against them manufactured and incorporated into the polyclonal ASV specific to that region.

Legislative

(*i*) Venomous snakebite to be made a notifiable disease.

(*ii*) ICD coding be used for all snakebite entries, thus assuring for a more realistic figure as to the number of bites and deaths.

(*iii*) Include a chapter on snakes in the Class VII or VIII texts of schoolchildren to help create awareness on snakes, snakebite and identification of common venomous species.

(*iv*) Taking venomous snakebite off the MLC (medico legal case) category other than in special situations.

Medical and diagnostics

(*i*) Snakebite and management be given due importance both by the government, research agencies and in the medical curriculum.

(*ii*) All cadre of healthcare professionals including the paramedics at all health facilities should be oriented to the snakebite identification, first aid and initial management and indications for immediate referral to higher centre for prevention of morbidity and mortality.

(*iii*) SVDK be developed by using any of the available methods – ELISA, lateral flow, optical immunoassay, fluorescence immunoassay, reverse latex agglutination, polymerase chain reaction-based assays, Aptamer-based assays *etc.* The major disadvantage of the syndromic approach is that treatment starts only after envenomation is confirmed from the signs and symptoms of systemic toxicity, which happens after the venom has already bound to receptors in tissues. ASV neutralizes only the free fractions of venom in the blood and does not have an effect on venom fractions which have been bound to tissue. With an SVDK, we would be able to confirm the presence of venom from a swab from the bite site even immediately after the bite, which would help identify the biting species. Presence of venom fractions in the urine or blood sample could help ascertain systemic envenomation. This could also help distinguish between non-venomous, venomous and dry bites.

(*iv*) Availability of an SVDK would also help ascertain as to which species has inflicted the bite, which would pave the way for the availability and manufacturing of monovalent ASV in the future. Treatment with monovalent ASV would help decrease the quantum of ASV being used, thereby decreasing adverse reactions as also making the treatment far more effective and concerted.

(*v*) Sharing of the Ministry of Health & Family Welfare-formulated guidelines in the management guidelines of snakebite to all public and private hospitals for uniform implementation for the management of snakebites.

(*vi*) Including treatment of snakebite into the mainstream curriculum of either internal medicine or emergency medicine and means of preventing snakebite in the community medicine curriculum.

(*vii*) Making it mandatory that all MBBS graduates be trained in life support skills as a part of their curriculum.

(*viii*) Carrying out a comprehensive epidemiological study to assess the burden of snakebite Pan-India.

(*ix*) Include venomous snakebite in the *Pradhan Mantri Jan Arogya Yojana* (PMJAY) scheme irrespective of the fact as to whether the victim has a PMJAY card or not.

Awareness and media outreach

(*i*) Appropriate information on snakes, snakebite prevention and first-aid should be shared with all the vulnerable groups through campaigns, social media and public broadcasting.

(*ii*) Basic preventive measures of snakebite including Do's and Dont's such as wearing footwear, using a flashlight and a walking stick at night, not putting ones hand into holes in the ground, keeping the premises and the boundary of the house clear from litter/grass, keeping the hen coop and shed a little distance from the house, not stacking firewood against the side of the house and doing so some distance away and using a mosquito net well tucked in under the mat while sleeping at night are some of the easily implementable measures to prevent snakebite at home.

(*iii*) Spreading awareness of the fact that the only treatment for venomous snakebite is ASV and there is no scientifically validated alternate form of treatment. Also highlighting that in case if bitten, one should be taken to the hospital as fast as possible.

(*iv*) Setting up a 24×7 snakebite helpline to answer queries with relation to snakes and snakebite.

A concerted effort on the part of all concerned namely policymakers, health authorities, public servants, ASV manufacturers, forest departments and health caregivers including treating doctors, non-governmental organizations, basic scientists, herpetologists and the lay public would lead to a fall in mortality and morbidity related to this eminently preventable cause of death and disability. It is also with the firm belief and knowledge that if the victim is treated early and properly, he/she would be leading a normal productive life. It also needs to be highlighted that various States pay a compensation amount of between ₹100,000 and 400,000 in case of death due to snakebite, which would in effect drain the exchequer off ₹5000-10000 million per year if claimed. A fraction of the amount if spent towards mitigation would help change the demographics of the disease from what it is today, for the better, in a few years from now.

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References

1. Alirol E, Sharma SK, Bawaskar HS, Kuch U, Chappuis F. Snake bite in South Asia: A review. *PLoS Negl Trop Dis* 2010; *4* : e603.
2. Menon JC, Joseph JK, Jose MP, Dhananjaya BL, Oommen OV. Clinical profile and laboratory parameters in 1051 victims of snakebite from a single centre in Kerala, South India. *J Assoc Physicians India* 2016; *64* : 22-9.
3. Punde DP. Management of snake-bite in rural Maharashtra: A 10-year experience. *Natl Med J India* 2005; *18* : 71-5.
4. Dandona R, Kumar GA, Kharyal A, George S, Akbar M, Dandona L. Mortality due to snakebite and other venomous animals in the Indian state of Bihar: Findings from a representative mortality study. *PLoS One* 2018; *13* : e0198900.
5. World Health Organization: Snakebite Envenoming. Available from: *https://www.who.int/news-room/fact-sheets/detail/snakebite-envenoming*, accessed on February 23, 2020.
6. Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, *et al*. The global burden of snakebite: A literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med* 2008; *5* : e218.
7. Suraweera W, Warrell D, Whitaker R, Menon G, Rodrigues R, Fu SH, *et al*. Trends in snakebite deaths in India from 2000 to 2019 in a nationally representative mortality study. *eLife* 2020; *9* : e54076.
8. Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, Jotkar RM, *et al*. Snakebite mortality in India: A Nationally representative mortality survey. *PLoS Negl Trop Dis* 2011; *5* : e1018.
9. Central Bureau of Health Intelligence: National Health Profile; 2019. p. 151-2. Available from: *http://www.cbhidghs.nic.in/showfile.php?lid=1147*, accessed on May 22, 2020.
10. Chippaux JP. Snakebite envenomation turns again into a neglected tropical disease! *J Venom Animalst Oxins Includ Trop Dis* 2017; *23* : 38.
11. Whitaker R, Captain A. Snakes of India, The Field Guide, Draco Books; 2008. Available from: *https://www.abebooks.com/9788190187305/Snakes-India-Field-Guide-Romulus-8190187309/plp*.
12. Whitaker R, Martin G. Diversity and Distribution of Medically Important Snakes of India. In: Gopalakrishnakone P, Faiz A, Fernando R, Gnanathasan C, Habib A, Yang CC, editors. *Clinical Toxinology in Asia Pacific and Africa. Toxinology*. Vol. 2. Dordrecht: Springer; 2015.

13. Majumder D, Sinha A, Bhattacharya SK, Ram R, Dasgupta U, Ram A. Epidemiological profile of snake bite in south 24 Parganas district of West Bengal with focus on underreporting of snake bite deaths. *Indian J Public Health*. 2014; *58* : 17-21.

14. Sarkhela S, Ghosh R, Mana K, Gantait K. A hospital based epidemiological study of snakebite in Paschim Medinipur district, West Bengal, India. *Toxicol Rep* 2017; *4* : 415-19.

15. Kochar DK, Tanwar PD, Norris RL, Sabir M, Nayak KC, Agrawal TD, *et al*. Rediscovery of severe saw-scaled viper (*Echis sochureki*) envenoming in the Thar desert region of Rajasthan, India. *Wilderness Environ Med* 2007; *18* : 75-85.

16. Joseph JK, Simpson ID, Menon NC, Jose MP, Kulkarni KJ, Raghavendra GB, *et al*. First authenticated cases of life-threatening envenoming by the hump-nosed pit viper (*Hypnale hypnale*) in India. *Trans R Soc Trop Med Hyg* 2007; *101* : 85-90.

17. Jayanthi GP, Veerabasappa Gowda T. Geographical variation in India in the composition and lethal potency of Russell's viper (*Vipera russelli*) venom. Toxicon 1988; 26 : 257-64.

18. Sharma M, Gogoi N, Dhananjaya BL, Menon J, Doley R. Geographical variation of Indian Russell's viper venom and neutralization of its coagulopathy by polyvalent antivenom. *Toxin Rev* 2014; *33* : 15-7.

19. Senji Laxme RR, Khochare S, de Souza HF, Ahuja B, Suranse V, Martin G, *et al*. Beyond the 'big four': Venom profiling of the medically important yet neglected Indian snakes reveals disturbing antivenom deficiencies. *PLoS Negl Trop Dis* 2019; *13* : e0007899.

20. Whitaker R, Whitaker S. Venom, antivenom production and the medically important snakes of India. *Curr Sci* 2012; *103* : 635-43.

21. Hawgood BJ. Doctor Albert Calmette 1863-1933: founder of antivenomous serotherapy and of antituberculous BCG vaccination. *Toxicon* 1999; *37* : 1241-58.

22. The Irula Snake Catchers' Industrial Cooperative Society. Available from: *https://madrascrocodilebank.org/web/the_irulas*, accessed on February 7, 2020.

23. Mukherjee AK, Maity CR. Biochemical composition, lethality and pathophysiology of venom from two cobras-- *Naja naja* and *N. kaouthia*. *Comp Biochem Physiol B Biochem Mol Biol* 2002; *131* : 125-32.

24. Chanda A, Patra A, Kalita B, Mukherjee AK. Proteomics analysis to compare the venom composition between *Naja naja* and *Naja kaouthia* from the same geographical location of Eastern India: Correlation with pathophysiology of envenomation and immunological cross-reactivity towards commercial polyantivenom. *Expert Rev Proteomics* 2018; *15* : 949-61.

25. Choudhury M, McCleary RJR, Kesherwani M, Kini RM, Velmurugan D. Comparison of proteomic profiles of the venoms of two of the 'Big Four' snakes of India, the Indian cobra (*Naja naja*) and the common krait (*Bungarus caeruleus*), and analyses of their toxins. *J Int Soc Toxinology* 2017; *135* : 33-42.

26. World Health Organization. *WHO guidelines for the production, control and regulation of snake antivenom immunoglobulins; 2018*. Available from: *https://www.who.int/bloodproducts/snake_antivenoms/snakeantivenomguide/en/*, accessed on December 15, 2019.

27. Wildlife Protection Act; 1972. Available from: *http://legislative.gov.in/sites/default/files/A1972-53_0.pdf*, accessed on March 12, 2020.

28. Regional Office for South-East Asia, World Health Organization. *Guidelines for the Management of Snakebites*. 2nd ed. 2016: WHO Regional Office for South-East Asia; Indraprastha Estate, Mahatma Gandhi Marg, New Delhi.

29. Standard Treatment Guidelines on the Management of Snake Bites. Ministry of Health & Family Welfare, Government of India; 2016. Available from: *https://nhm.gov.in/images/pdf/guidelines/nrhm-guidelines/stg/Snakebite_QRG.pdf*, accessed on July 24, 2020.

For correspondence: Dr Joy Kumar Chakma, Division of Non-Communicable Diseases, Indian Council of Medical Research, New Delhi 110 029, India
e-mail: drjkna@yahoo.com