

Cross-sectional survey of the incidence, mortality and socioeconomic burden of snakebite envenoming in India

Corresponding Author: Dr Jaideep Menon

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Attachments originally included by the reviewers as part of their assessment can be found at the end of this file.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

Thank you for the opportunity to review this manuscript.

Snakebite has long been a severely neglected disease, not only in India but globally, until very recently. Most victims come from marginalized rural agricultural communities, and the deaths and disabilities caused by snakebites are largely preventable. While governments have remained largely silent on the issue, the scientific community has made significant efforts to explore the epidemiology of this neglected disease and advocate for necessary public health measures. It is encouraging to see the Indian government take action by establishing a national task force under the purview of the Indian Council of Medical Research (ICMR), the country's premier institution responsible for shaping public health policy. I sincerely appreciate the hard work of the ICMR team in undertaking this critical task, and I am pleased to provide my comments on the findings of the manuscript by Menon et al., submitted to Nature Communications.

1. I see this study builds upon the research protocol previously published in PLOS ONE in 2022. As outlined in their original protocol, study is a multi-center investigation aimed at determining the incidence, morbidity, mortality, and economic burden of snakebites in India. Covering all five geographical zones of the country, the study spans 13 states and provides state-specific estimates on snakebite incidence, mortality rates, injury patterns, healthcare-seeking behaviors, and the associated cost of illness among victims.

2. I suggest authors should look back again to review what you have been achieved and not achieved from your original plan. Please explain if any specific reasons to exclude state specific estimates, DALY's etc..

3. In the study protocol (Menon et al. 2022; Table 2), the authors anticipated significantly higher snakebite rates. I have a strong concern regarding the substantial discrepancy between the anticipated and actual death and incidence rates reported in this study. Do you have any explanation for this difference?

a. Anticipated Incidence: 84,000 cases → Reported: 7,094 cases (only 8%)

b. Anticipated Deaths: 5,039 deaths → Reported: 195 deaths (only 4%)

4. The way Table 2 presents sounds to me that all the species related to bites were recognized. "Other Venomous Species" is considerably a large group. Would you be able to further classify to see what other medically important species are therein.

5. Table 4 describes 84% of 7,094 cases were sought hospital treatment and 57% of 196 reported deaths occurred in health facilities. Suraweera et. al. 2020 found a large number of snakebites were never reported to hospitals and 2 out of every 3 snakebite deaths were occurring out of the hospitals. Findings of this study are very different from previous findings. How do you defend the accuracy of your data?

6. Could you elaborate the data quality assessment of ASHA workers? Especially, have you done any follow up evaluation to assess the completeness of data collection to identify any potential underreporting of snakebite cases or deaths from them?

7. The study protocol describes the data collection period as 18 months (April 2022 – October 2023). However, in the discussion section (Lines 384–389), the authors mention that data collection was disrupted by the COVID-19 pandemic, but there is no specific information on how the timeline was adjusted or if data collection periods varied across districts. For greater transparency, could you add an additional column to Table 7 to indicate the specific data collection period for each district?

8. The use of the term "risk" to describe mortality and incidence rates in this study is somewhat confusing to me. In a cross-sectional study, a more precise description would be mortality rate and incidence rate rather than "risk". Also you can consider the term Antivenom instead of Anti-Snake Venom in consistent with the same used by WHO and in scientific literature.

9. Line 384: I could not locate an explanation for "NTF study". Could you clarify what this term refers to?

Reviewer #2

(Remarks to the Author)

I found the present article very useful for public health community and a very relevant step towards the goal of reducing snakebite incidence by 50% by 2030. Nevertheless I have some reservations when it comes to certain estimates, how suitable it is to be published in Nature Communications, since it is at the moment a descriptive study and as the title suggests it is an interim report for which more data will be collected at an unspecified time from two pending districts. Below are specific comments on the different aspects of the article the journal suggests the review should focus on.

Quality of the data.

I believe the collected data are very useful for certain purposes such as identifying demographic and occupational risk factors, their proportional burden on the different gender, age and income groups, even including the different snakebite envenoming diseases. For estimating incidence I believe the data are relatively poor, as estimating the population at risk is problematic with the methods used (more comments on this later).

Level of support for the conclusions.

This paper is more of a project report than an investigation into proving a hypothesis or gather evidence in support of a theory. As such there are no conclusions based on statistical hypothesis tests.

Potential significance of the results.

The results I believe will be very useful for public health stakeholders, and will also prove useful for future research on snakebite eco-epidemiology, as in the long run, even though this is a cross-sectional study, several parameters relevant to its temporal patterns can be derived which will motivate several quantitative research initiatives.

Key results

A very detailed unfolding of snakebite cases improves understanding of the level of complexity and interplay between risk factors, snake species and co-morbidities.

Validity

I don't think there is any effort made to interpret data. This work is only a report of raw data findings which will have to be analysed in greater detail in the years to come. As stated above, there are inherent limitations to the sampling strategy, mainly, that actual incidence figures cannot be as easily calculated as shown in the manuscript. A better approach would have to be to use an estimate of the population under the watch of each participating ASHA.

Significance

Even though there has not been a deep analysis yet, the collected data will be used in many analyses, and potentially serve as an example to be replicated by nations where snakebite is a pressing issue, also potentially resulting in large scale analysis and modelling that will help solve the snakebite crisis.

Data and methodology

This is a data article, so as mentioned before, even though it represents a massive effort, there are important limitations related to the unknown size of the population at risk under the watch of the survey technicians. Sample size is initially compared with that of a nation-wide community survey from Sri Lanka, suggesting that this has been an improved, upscaled effort, although this is far from true. The sampling design focuses on detection of snakebite cases only, where their reporting is voluntary. In contrast, the Sri Lankan data set is a survey of randomly selected households to respond a set of questions focusing on the occurrence of snakebite and envenoming cases. Therefore, the main difference is that incidence rates in the latter can be estimated using the survey population, although as mentioned above this study's strength is that it allows very detailed unfolding of risk factors, which had not been available before.

Suggested improvements.

I believe the paper will mainly benefit from a more cautious communication of the data-sets' weaknesses, which as I also mention above are compensated with a level of epidemiological detail never seen before among snakebite studies. Also, the fact that "incidence" estimates are at the forefront of this work, and for the reasons stated above these are dubious, it should be eliminated from the title, and then mention that estimating incidence rates is possible with a careful estimation of the

survey's population at risk.

Version 2:

Reviewer comments:

Reviewer #2

(Remarks to the Author)

I do not have any further comments on this project and welcome its publication. I think the team of authors have done an excellent job at addressing review comments.

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Response to the Reviewers

We thank the reviewers for their meticulous review and insightful comments. In the following section we have presented the responses to the comments raised and also indicated the revisions made in the manuscript with page and line numbers.

Reviewer #1 (Remarks to the Author):

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2. I suggest authors should look back again to review what you have been achieved and not achieved from your original plan. Please explain if any specific reasons to exclude state specific estimates, DALY's etc.

We thank the reviewer for raising this important comment.

We would like to submit that the study is ongoing with data collection continuing in two states. In a subsequent paper, we plan to address the objectives stated in the protocol with state specific estimates, DALY using the disability weight for poisoning as a surrogate, and state-specific contexts or situations leading to snake-human conflict as also outcomes secondary to snakebite envenoming based on time delays to treatment and on the health seeking behaviour. This has been explained in the discussion section of the paper in pages 14-15.

"The ICMR-funded National Task Force study is, hence, the only nationally representative, at scale, community-based study assessing incidence, mortality, treatment-seeking behaviour, therapy and the economic burden of snakebites across the country. In this interim report of the ongoing study, we present the mortality rate due to snake bite and the economic burden suffered by the patients. Subsequently, in the final report, we intend to present state-specific estimates and quantify the morbidity burden of snakebite using Disability Adjusted Life Years (DALYs), using the disability weight for poisoning as a surrogate following the methodology followed by Kasturiratne et al. (2017), in

measuring economic burden of snake bites in Sri Lanka (Kasturiratne A, Pathmeswaran A, Wickremasinghe AR, et al.: The socio economic burden of snakebite in Sri Lanka. PLoS Negl Trop Dis. 2017; 11(7): e0005647).”

3. In the study protocol (Menon et al. 2022; Table 2), the authors anticipated significantly higher snakebite rates. I have a strong concern regarding the substantial discrepancy between the anticipated and actual death and incidence rates reported in this study. Do you have any explanation for this difference?

a. Anticipated Incidence: 84,000 cases → Reported: 7,094 cases (only 8%)

b. Anticipated Deaths: 5,039 deaths → Reported: 195 deaths (only 4%)

We agree with the reviewer that the difference between the anticipated deaths and the deaths reported in the study needs to be examined.

The anticipated incidence of snakebite was calculated using incidence taken from the study by Majumder et.al. Epidemiological studies in area are scarce and we went by the only contextual, contemporary data available which was from the single state of West Bengal. Nevertheless, we agree that the reported incidence seems small as a number of snakebites could have gone unreported. We have revised the discussion section to include this part in page number 15.

“The incidence of snakebite and mortality reported in the study is much lower than what was anticipated. The anticipated incidence of snakebite was calculated using incidence taken from the study by Majumder et.al.²⁰ Epidemiological studies in this area are scarce and hence we used the only contextual, contemporary data available which was from the single state of West Bengal. The considerably lower number of snakebite incidence could be attributed to significant underreporting of cases in India.”

The incidence of death was calculated as 6/100000 based on the data from the one-Million-Death Study (1-MDS). The number of deaths captured was only 4% of the estimate. The estimate of death from verbal autopsies as was done in the 1-MDS seems grossly overestimated as compared to what we gathered from the community. For example, there were 31 deaths due to SBE in Kerala (population 35 million) for the year 2024-25, whilst based on the 1MDS estimate the number of deaths would have been 2100 for the state. Additionally, the methodological differences between the studies also need to be considered. This has been discussed in the revised paper in the methodology section (page 06) and discussion section (page 15).

“The districts were purposefully selected to reflect India’s diverse geographical and ecological terrains coastal, forest, highland, and plains, as outlined in the study protocol. This approach prioritised contextual representativeness over statistical randomness to better capture variations in risk factors across different settings (page 06).”

“The anticipated mortality for the study was estimated to be 6/100000 based on the data from the mortality reported in one-Million-Death Study (1-MDS) (<https://pmc.ncbi.nlm.nih.gov/articles/PMC3075236/>). However, with a mortality rate of 0.33%, the number of deaths captured in our study was only 4% of the anticipated estimate. In case of snakebite, the estimate of death in the 1-MDS appears to be grossly overestimated as compared to what we have gathered from the community. For example, there were 31 deaths due to SBE in Kerala (population 35 million) for the year 2024-25, whilst based on the 1-MDS estimate the number of deaths would have

been 2100 for the state. The 1-MDS study was a prospective, nationally representative study to estimate cause-specific mortality using Verbal Autopsy (VA). Our study was a community-based cross-sectional study specifically aimed to estimate the incidence and mortality from snakebite across five different biospheres in India to capture the diversity of biting species. Although VA has significantly strengthened the mortality monitoring system in India, it carries the potential for misclassification and over or under estimation of deaths in case of conditions without a well-defined set of signs and symptoms such as snakebite (<https://pmc.ncbi.nlm.nih.gov/articles/PMC7590499/#:~:text=The%20method%20has%20shown%20to,deaths%20occurring%20in%20Maputo%2C%20Mozambique>) (page 15)."

4. The way Table 2 presents sound to me that all the species related to bites were recognized. "Other Venomous Species" is considerably a large group. Would you be able to further classify to see what other medically important species are therein.

We thank the reviewer for pointing this out. However, all biting species were not identified, with 14.7% not reporting the biting species. The biting species vary considerably across different geographical areas including monocellate cobra, hump-nose pit viper, green pit viper, mountain pit viper, and other such species relevant to geography. Although identification of all medically important species would carry significant value, it would be beyond the scope of our study to be available to identify all the species which have led to snakebite especially for the north-eastern and northern parts of the country.

5. Table 4 describes 84% of 7,094 cases were sought hospital treatment and 57% of 196 reported deaths occurred in health facilities. Suraweera et. al. 2020 found a large number of snakebites were never reported to hospitals and 2 out of every 3 snakebite deaths were occurring out of the hospitals. Findings of this study are very different from previous findings. How do you defend the accuracy of your data?

We understand the concern raised. However, considering the methodological differences between the two studies, it would not be a robust comparison. Ours is a community-based primary empirical research study which estimated the incidence of snakebite as well as mortality, whereas the study by Suraweera et al based the findings on the analysis of 2833 snakebite deaths from 611,483 verbal autopsies in the nationally representative Indian Million Death Study from 2001 to 2014, and conducted a systematic literature review from 2000 to 2019 covering 87,590 snakebites. We would also like to submit that out of the 196 deaths reported in our study, 43.08% were reported as out-of-hospital, either at home or while during transit to a healthcare facility, which is along the lines of what is generally reported from Suraweera et al, as well as other studies from low-middle-income-countries like Sri Lanka or India.

6. Could you elaborate the data quality assessment of ASHA workers? Especially, have you done any follow up evaluation to assess the completeness of data collection to identify any potential underreporting of snakebite cases or deaths from them?

Data quality assessment of ASHA workers is a critical issue. For each death reported, the field officers went to the house of the victim to understand better the contexts which led to the snake-human conflict and death. Additionally, telephonic verification was done for each 10th bite reported from a single participatory site (district) by the district coordinator of the district. We also compared data with

compensations paid by the State Forest department for each death reported secondary to SBE. This has now been added in the paper in the methodology section in page number 7.

“For each death reported, the field officers visited the victim’s house to understand the contexts which led to the snake-human conflict and consequent death. Additionally, telephonic verification was done for each 10th bite reported from a single participatory site (district) by the district coordinator of the district. We also compared data with compensations paid by the State Forest department for each death reported secondary to SBE.”

7. The study protocol describes the data collection period as 18 months (April 2022 – October 2023). However, in the discussion section (Lines 384–389), the authors mention that data collection was disrupted by the COVID-19 pandemic, but there is no specific information on how the timeline was adjusted or if data collection periods varied across districts. For greater transparency, could you add an additional column to Table 7 to indicate the specific data collection period for each district?

Each of the different states collected data for a continuous period of 1 year, though many of the states had different start lines to the study. We have now added an Annexure column giving the data collection period specific to the state.

State	District	Study Period
Andhra Pradesh	Chittoor	January 2022- December 2023
Arunachal Pradesh	Pakke Kessang	May 2023-April 2024
	Papum Pare	May 2023-April 2024
Himachal Pradesh	Chamba	May 2022- April 2023
	Kangra	April 2023- March 2024
	Una	May 2022- April 2023
Kerala	Ernakulam	February 2022- January 2023
	Kannur	September 2022- August 2023
Maharashtra	Nanded	February 2022- January 2023
	Pune	February 2022- January 2023
	Raigad	June 2022-May 2023
Mizoram	Aizawl	April 2023- March 2024
	Champhai	June 2023-May 2024
	Lunglei	June 2023-May 2024
Odisha	Cuttack	April 2022- March 2023
	Sambalpur	April 2022- March 2023
Punjab	Amritsar	April 2023- March 2024
	Hoshiarpur	April 2023- March 2024
	Ludhiana	April 2023- March 2024
Rajasthan	Bikaner	September 2021- August 2022
	Jaisalmer	September 2021- August 2022
	Udaipur	September 2021- August 2022
Tripura	Dhalai	February 2023- January 2024
	South Tripura	February 2023- January 2024

8. The use of the term "risk" to describe mortality and incidence rates in this study is somewhat confusing to me. In a cross-sectional study, a more precise description would be mortality rate and incidence rate rather than "risk". Also, you can consider the term Antivenom instead of Anti-Snake Venom in consistent with the same used by WHO and in scientific literature.

We agree that the term rate better explains incidence and mortality than risk and the same has been incorporated as suggested

9. Line 384: I could not locate an explanation for "NTF study". Could you clarify what this term refers to?

We apologize for the oversight. We have now expanded it to 'National Task Force'.

Reviewer #2 (Remarks to the Author):

I found the present article very useful for public health community and a very relevant step towards the goal of reducing snakebite incidence by 50% by 2030. Nevertheless, I have some reservations when it comes to certain estimates, how suitable it is to be published in Nature Communications, since it is at the moment a descriptive study and as the title suggests it is an interim report for which more data will be collected at an unspecified time from two pending districts. Below are specific comments on the different aspects of the article the journal suggests the review should focus on.

Quality of the data.
I believe the collected data are very useful for certain purposes such as identifying demographic and occupational risk factors, their proportional burden on the different gender, age and income groups, even including the different snakebite envenoming diseases. For estimating incidence, I believe the data are relatively poor, as estimating the population at risk is problematic with the methods used (more comments on this later).

We thank the reviewer for acknowledging the value of the dataset in exploring demographic, occupational, and clinical risk factors. We agree that the approach to estimating incidence differs from that of household surveys. However, as clarified in below, the projected district population was used as the denominator of the population at risk. The study was planned as a community study primarily to account for victims of snakebite who did not seek medical care or did so with alternate treatment / faith healers. The data gathering was at 'ward' level (a ward is the smallest administrative subunit of a village / town), by ASHA workers. Keeping in mind that each ward is served by an ASHA who functions as the eyes and ears of the health department in the community. This community-level coverage through trained ASHAs provides a reasonable basis for estimating district-level incidence as ASHAs in general are well aware of health issues in their wards (typically a population of 1200-1500, or 250-350 households).

This has been incorporated into the paper for further clarity in the methodology section under the sub-section of data collection in page 7.

“Data was collected by trained frontline health workers (ASHAs) at the ward level, which is the smallest administrative subunit of a village / town, and the projected district population was used as the denominator of the population at risk. In India, the ASHA workers serve as the eyes and ears of the healthcare system and are typically aware of the acute health events in their communities. They reported new snakebite cases within two weeks of the incident, hospital visit, discharge status from hospital, or death, regardless of whether the victim sought treatment in a hospital or through alternative methods. The community-level coverage through trained ASHAs provides a reasonable basis for estimating district-level incidence as ASHAs in general are well aware of health issues in their wards (typically a population of 1200-1500 from 250-350 households). Since all wards in a district are covered by at least one ASHA depending on the population size, the entire district population would naturally be under ASHA coverage, justifying the projected district population as the population at risk for SBE.”

Level of support for the conclusions.
This paper is more of a project report than an investigation into proving a hypothesis or gather evidence in support of a theory. As such there are no conclusions based on statistical hypothesis tests.

I agree with the reviewer in that this study was never planned for generating a hypothesis or causality. The primary aim was descriptive—to quantify and detail the burden, clinical course, and economic aspects of snakebite which had never been done before at scale in the country with the largest burden of snakebite. The learnings from this study includes that over 40% of victims of snakebite lose their lives outside hospital settings, victims bitten were predominantly below-the-poverty line and that 88% of victims did not have any insurance cover. Based on the social, demographic, geographical, climatic and environmental factors we would be hypothesising on factors responsible for snake-human conflict, alongside creating hotspot maps for the study districts.

Potential significance of the results.
The results I believe will be very useful for public health stakeholders, and will also prove useful for future research on snakebite eco-epidemiology, as in the long run, even though this is a cross-sectional study, several parameters relevant to its temporal patterns can be derived which will motivate several quantitative research initiatives.

Key results
A very detailed unfolding of snakebite cases improves understanding of the level of complexity and interplay between risk factors, snake species and co-morbidities.

Validity
I don't think there is any effort made to interpret data. This work is only a report of raw data findings which will have to be analysed in greater detail in the years to come. As stated above, there are inherent limitations to the sampling strategy, mainly, that actual incidence figures cannot be as easily calculated as shown in the manuscript. A better approach would have to be to use an estimate of the population under the watch of each participating ASHA.

We would like to clarify that the Accredited Social Health Activists (ASHAs) are designated community-level health volunteers under India's public health system. Each ASHA is assigned to a specific ward—the smallest administrative unit in a district—with the responsibility of overseeing health-related activities for the ward population.

For this study, all ASHAs in the selected districts were comprehensively trained and actively engaged in prospective case identification and reporting. As each ward has a designated ASHA who is closely connected to the community, and since every ASHA in the participating districts was included, we consider the entire district population to be under surveillance. Therefore, the denominator for our estimates is the district population, which we believe appropriately reflects the population at risk in the context of our study design.

Significance

Even though there has not been a deep analysis yet, the collected data will be used in many analyses, and potentially serve as an example to be replicated by nations where snakebite is a pressing issue, also potentially resulting in large scale analysis and modelling that will help solve the snakebite crisis.

Data and methodology

This is a data article, so as mentioned before, even though it represents a massive effort, there are important limitations related to the unknown size of the population at risk under the watch of the survey technicians. Sample size is initially compared with that of a nation-wide community survey from Sri Lanka, suggesting that this has been an improved, upscaled effort, although this is far from true. The sampling design focuses on detection of snakebite cases only, where their reporting is voluntary. In contrast, the Sri Lankan data set is a survey of randomly selected households to respond a set of questions focusing on the occurrence of snakebite and envenoming cases. Therefore, the main difference is that incidence rates in the latter can be estimated using the survey population, although as mentioned above this study's strength is that it allows very detailed unfolding of risk factors, which had not been available before.

As clarified earlier, the ASHA and the population under their watch are integral to our surveillance approach. ASHAs (Accredited Social Health Activists) are community-based health workers designated to each ward, the lowest administrative unit in a district and are responsible for maintaining close and continuous engagement with the population in that area. Since each ASHA was trained and included in this study, and all wards in the selected districts were covered, we consider the district population as the effective population under surveillance, thereby justifying our use of district-level population as the denominator.

Additionally, the selection of districts was not based on incidence rates alone. Rather, districts were purposefully selected to represent the diversity of India's geographical and ecological terrains- including coastal, forest, highland, and plain regions as outlined in our study protocol. This approach was intended to ensure geographic and ecological representativeness rather than statistical randomness, which is more appropriate for capturing variations in risk factors and contextual nuances.

While we acknowledge that our methodology differs from that of the Sri Lankan national household survey, the design of our study- based on active, real-time case identification through embedded community health workers provides unique strengths, particularly in enabling the detailed documentation of risk factors, health-seeking behaviour, and health system responsiveness that are often not captured in household surveys.

Suggested improvements.

I believe the paper will mainly benefit from a more cautious communication of the data-sets' weaknesses, which as I also mention above are compensated with a level of epidemiological detail never seen before among snakebite studies. Also, the fact that "incidence" estimates are at the forefront of this work, and for the reasons stated above these are dubious, it should be eliminated from the title, and then mention that estimating incidence rates is possible with a careful estimation of the survey's population at risk.

As earlier clarified, the use of the term "incidence" is based on the justified assumption that the entire district population was under surveillance through trained ASHAs for a specified period of 1 year of data collection, each responsible for a specific ward. While we agree that national-level incidence estimates are beyond the study's scope, the district-level incidence rates derived from prospective community-based surveillance are valid within this context. Each ward is represented by an ASHA. So, the entire population is under ASHA watch.

Reviewer report : "ICMR-National Task Force Project: Incidence, mortality and socioeconomic burden of snakebite in India, an interim report" by Menon et al. - Nature Communications.

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9. **Line 384:** I could not locate an explanation for **"NTF study"**. Could you clarify what this term refers to?

This research represents a significant step forward in understanding and addressing the burden of snakebites in India. I look forward to further discussions on its findings and implications for public health policy.