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Letter to the editor

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* Suhita R, Begum I, Rashid M, Chandran V, Shastri S, Kantamneni R, et al. Systematic review and meta-analysis of global prevalence of neurotoxic and hemotoxic snakebite envenomation. East Mediterr Health J. 2022;28(12):909–916. https://doi.org/10.26719/emhj.22.090 .

Dear Editor,

In an article published by EMHJ Vol. 28 No. 12 of 2022, Suhita et al. attempted a systematic review and meta-analysis of the prevalence of neurotoxic and hemotoxic snakebites globally (1). The authors used the right resources for the review but erred in using systematic review to answer an epidemiological question that is not amenable to this method. The result is the

spurious conclusion that North America has the highest prevalence of hemotoxic and neurotoxic snakebites in the world. Their conclusions conflict with WHO data showing that the burden falls most heavily in Asia and Africa (2,3).

They reviewed 35 articles from USA and overlooked other North American snakebite literature meeting their search criteria (4–9). Few of the articles cited measured prevalence by systematic data collection but described specific cohorts of patients defined by their envenomation or geography.

Sahita et al. leaned heavily on the North American Snakebite Registry (NASBR) of the Toxicology Investigators Consortium (10). NASBR primarily records snakebites in the desert southwest where rattlesnakes predominate, and two-thirds of these snakebites come from 6 states (44% from Arizona alone). Two-thirds of identified snakes were rattlesnakes, but America's Poison Centers consistently recorded twice as many copperhead bites as rattlesnake bites (11–13). Arizona contributes only 6% of snakebites (6).

The authors seem to assume that publication frequency indicates prevalence within the country of origin. Estimates of snakebites in the US range from 7000 to 10 000 per year among a population of just over 333 million inhabitants (6,14). This is an incidence of approximately 1 in 33 000–48 000 persons per year. Prevalence represents the number of persons with the condition of interest at a given time. Since neurotoxicity and hemotoxicity are usually not permanent conditions after venomous snakebite, the prevalence of these 2 effects of snakebite are much lower.

These 7000–10 000 US snakebites per year are about 0.2% of the global total estimated snakebites. Copperhead (Agkistrodon contortrix) snakebites account for over half of the US total of venomous snakebites, and these characteristically have little or no haemotoxicity (15,16) or neurotoxicity. Among the snakebites occurring in the US, the proportion of snakebites with hemotoxicity should be well below 50%. Thus, the annual "prevalence" estimate should be well below 0.15% of the population.

Frequency of publications in a country may depend upon local resources. Only 4 of the articles reviewed were from Africa, while 35 were from the USA. Kasturiratne et al. found a similar publication bias in a more credible estimate of venomous snakebite injuries and deaths (17).

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Response by authors of the paper

Thank you so much for your valuable time and efforts to read and comment on our manuscript entitled "Systematic review and meta-analysis of global prevalence of neurotoxic and hemotoxic snakebite envenomation".

Systematic reviews are the gold standard to search for, collate, critique, and summarize the best available evidence regarding a clinical question (1). There are many published systematic reviews of prevalence and we provide reference to 2 most prominent methodological studies to show that systematic reviews can be conducted to answer epidemiological questions such as prevalence (1,2).

In systematic review, evidence is synthesized by collating data from included studies and drawing conclusions from the synthesis only. In our review, we clearly mentioned that we have included only observational studies and randomized controlled trials (RCTs) published in English language and we excluded unpublished data and WHO reports. Our conclusion was based on the pooled prevalence of included studies (3), which may not be aligned with WHO report.

To identify the geographical distribution of snakebite, we categorized the results by continent and presented the results. Based on our study, the highest pooled prevalence of snakebite was in North America.

WHO categorized snakebite envenomation as a neglected tropical disease and reported that most of the snakebites occur in Africa, Asia and Latin America (4). WHO and US CDC (5,6) use multiple sources for monitoring health indices, including published studies, unpublished data, online and offline survey reports, registries, as well as reports from government and non-government institutions. However, systematic reviews and meta-analysis consider specific populations based on predefined inclusion and exclusion criteria, and the results and conclusion will depend on findings from the studies. This may or may not represent the global statistics.

In our paper, we considered all the studies that met the prespecified inclusion criteria because it was a secondary research based on published studies. This included only RCTs and observational studies that discussed snakebite envenomation irrespective of other characteristics such as specific cohorts or geography. We included the North American study by Dart et al. (7) and the study by Ruha et al. (8) in our review, and excluded some others because they had no prevalence data (9); reported snakebite injuries and treatment, which did not represent actual prevalence data (10); did not provide an outcome of interest to our study (10,11); provided mixed reports on venomous snakes and lizards (12); and are annual reports which do not fall within our inclusion criteria (13–15). We did not include data from any specific snakebite databases of any country or region.

Systematic review synthesizes evidence from available literature based on criteria set by the researchers. Our findings were based on the reported outcomes and may or may not be the same as the US CDC, WHO or any other institution’s reports.

Our literature search identified maximum number of publications from India, Brazil, United States of America, and Sri Lanka. Hence, our pooled prevalence mostly relied on the individual study findings. Kasturiratne et al. (16) synthesized evidence from various published and unpublished sources and reported published literature on snakebite from USA, Australia, Columbia, Argentina, France, Nigeria, and Saudi Arabia and no published literature from most African and Asian countries.

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