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Renal Complications in Children with Hematotoxic Snakebite: More Information Needed

We read with interest the recent article on renal complications in children with hematotoxic snakebite by Islam, *et al*. [1]. We herein wish to raise some pertinent issues to assist in better understanding of this article.

(*i*) Though the aim of the study was to ascertain clinical and laboratory indicators predicting acute kidney injury (AKI) "early" in children with snakebite envenomation; these predictors have neither been mentioned in the results nor in tables, unlike an earlier study [2], where various clinical and laboratory parameters were reported as predictors.

(*ii*) There is no mention of baseline hemoglobin, maximum fall in hemoglobin, serum lactate dehydrogenase, evidence of myoglobinuria, hemodynamic status, cardiac dysrhythmias, cardiac dysfunction, evidence of adrenal hemorrhage, blood pressure, creatinine etc. which would have helped interpret the results better. These would have looked at creating a list of predictors of renal complications too [2]. Similarly, AKI could have been due to numerous other confounders like shock, dehydration, nephrotoxic antibiotics adminis-tration etc., which have not been detailed. Similarly, whether drug dose adjustments were made in those with AKI has also not been mentioned.

(*iii*) AKI was appropriately defined based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria [3]. However, these patients were then followed up for 6 months [1], the reason for which is not clear, because for labelling chronic kidney disease, a 3-month follow-up would have been enough.

(*iv*) Though one of the criteria for dialysis mentioned in this study was hyperkalemia, but the reason why medical management was not considered as an option is not apparent. Similarly, other reasons for dialysis like uremia, refractory metabolic acidosis too may have been indications for dialysis in these patients, which probably have not been included.

(*v*) It was mentioned in the methodology that "peritoneal dialysis was done in the institution and hemodialysis in a referral hospital". Whether these children were excluded or followed up is not clear. Details of how these children were followed up are missing. How many of these children who underwent dialysis developed 'permanent renal damage' at the 6-month follow up too has not been mentioned by authors, which could have been new information for the readers.

(*vi*) Similarly, it is not clear as to whether the authors had taken the AKI stage at presentation or the maximum AKI stage as per the KDIGO guidelines during the hospital stay.

(*vii*) What were the indications and timing for the renal biopsy? Was doing a renal biopsy in the setting of an AKI reasonably justified and ethically correct? Snake-bites being medicolegal cases, it looks improbable that a renal biopsy was possible in 100% of the children who died but in only 81.4% of those who survived.

(*viii*) It is mentioned that 59 out of 364 children (16.2%) had "permanent renal damage" [1]. This is inappropriate as the denominator should exclude the deaths as permanent renal damage can be assessed only in those who survived the episode. So, we feel that the 16 children who succumbed should have been excluded, thus increasing the percentage of children with permanent renal damage to 16.9%.

(*ix*) We presume that the median number of vials of anti-snake venom (ASV) used in both groups have been mentioned in Table I [1]. It may have been appropriate to have also mentioned the mean value, which would have added more clarity to the renal outcomes.

(*x*) In the results, the authors state "our model can correctly predict 67.2-78.9% variation in AKI and 53.1-61.7% variation in mortality." However, it is unclear which model they are referring to?

(*xi*) The authors have mentioned mean "bite to ASV administration time" as 36.4 (5.9) minutes which seems practically difficult as their study population included patients from faraway places like the neighboring states of Bihar and Jharkhand. Besides, the whole blood clotting time itself takes 20 minutes to process after which the ASV must have been administered as per standard practice, which further delays the time to ASV administration. Hence, the mentioned time does not appear to be possible in these settings, as also seen in a previous study from the same region where this interval was 270 minutes [4].

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AUTHORS' REPLY

We thank the readers for their interest in our study [1]. Our replies to the queries are as under:

(*i*) Different clinical and laboratory parameters were already described in table I and II of the article, and some of the determinants are similar to previous reports [2]. Reasons for discrepancy with published literature were mentioned in the discussion section of the article.

(*ii*) Detailed baseline data were collected, but all of it could not be presented due to limitation on the size of the manuscript. Serum LDH and adrenal hemorrhage were not assessed in our study. We appreciate your concern about cardiac dysfunction, hemodynamic status etc, but different parameters (requirement of ventilation, serum potassium level, requirement of inotropes) mentioned in table I act as surrogate markers of them. We used logistic regression and adjusted odds ratio to remove confounders. Nephrotoxic drugs are avoided in viper-bite patients according to unit protocol in our set-up.

(*iii*) In a previous research project in the same setting, the investigators noted some long-term toxicity of snakebite, as also previously reported [2]. Hence we decided on a follow-up period of 6 months.

(*iv*) In the paper, we had mentioned the unit protocol for dialysis. Opinion of a nephrologist was sought before starting dialysis in all patients.

(*v*) All study patients were followed up at our nephrology specialty clinic after discharge from hospital.

(*vi*) If at any point of time during the hospital stay, the children developed AKI, we included them in the AKI group. The initial version of the manuscript had information on AKI grades, but it was later edited out on the suggestion of reviewers.

(*vii*) We did not perform renal biopsy in AKI settings. We considered renal biopsy in the children who developed permanent renal damage, as per opinion of nephrologist. Before doing renal biopsy, we took informed written consent from parents.

Snake bite, being a medicolegal case, autopsy is done in every death. Samples from viscera are also routinely collected by forensic expert. We could convince parents of all such children for consent for renal histopathology examination.

(*viii*) We used the study population as denominator because we want to identify renal complication in children with hematotoxic bites, not in the surviving children.

(*ix*) As the data are skewed, we had summarized it as median and interquartile range [1]. The mean (SD) number of vials required were 12.3 (9.1) and 21.5 (18.9) in AKI and no AKI groups, respectively.

(*x*) It is the regression model used in the study.

(*xi*) The mentioned time is only for those who did not develop AKI; it was higher for those who developed