Peer Review File

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Reviewer A

The study investigates the diagnostic consistency, incidence, and mortality rate, clinical signs, and influencing factors of renal injury related to sepsis in children.
diagnosed by three different AKI diagnostic criteria, then evaluated which was more valuable.
1. The entire article should be reviewed for completeness of expression and grammar, and more scientific language should be used. (line 169, combined blood system disease; line 200, infectious shock)
Reply: We have modified our comment as advised(see page 2, line 49-50, 51-53; page 4, line 104-106, 51-53；page 5, line132；page 7, line 187，193，196; page 8, line 220; page 9, line 267-271，273; page 10, line 275-277,302,304; page 11, line 307, 321-323,327,328,330,331,333-335; page 12, line 336-338,342-347,358-359; page 13, line 308-382,387,390).

2. New sepsis diagnostic criteria were published in January 2024, and MAP values were determined according to age. According to these criteria, the definition of "severe sepsis" has been abolished. Using median MAP values in a study with patients from different age groups is not appropriate. Defining patients' sepsis/septic shock according to new criteria in the light of current literature will increase the timeliness of the article.
Reply: We have modified our comment as advised(see page 4, line105, page 7, line 211-212; page 8, line 213;page 15, line 450-453).

3. The discussion section needs to be revised and the references of the mentioned sources must be added.
Reply: We have modified our comment as advised(see page 15, line 450-453; page 17, line 500-504)

4. On which day of hospitalization were patients diagnosed with SA-AKI?
Reply: We have modified our comment as advised **(see page 5, line 132).**
All suggested corrections and questions have been added to the file.

Reviewer B

The study aim is specific and well targeted. The research concept is great, but it requires better statistical review and analysis. Execution of the study aim/objectives needs a lot of review and refinement.
The authors should specifically state what is new from their study (line 13 – 21). It is not explicit as they stated what is known and what is new together making it difficult for readers to differentiate which is which.
Reply: We have modified our comment as advised(see page 1, line28-29; page 2, line30-31).

Methods

Please is the study a retrospective cohort study or retrospective cross-sectional study? There is no evidence suggestive of retrospective follow up of the exposure variables that led to the outcome SA-AKI but rather a snapshot of the independent/exposure variables with outcome variable was done. For cross sectional study, outcomes and exposures are measured at the same time. The exposure variables in this study were not longitudinally measured but were measured as a snapshot of exposure variables obtained when the patients had SA-AKI.

Reply: the study is a retrospective cohort study.

Please what is the definition of sepsis-associated AKI (SA-AKI)? This should be stated in the methods. How was sepsis determined and what were the evidence on the use of diagnostic criteria? The authors should have what they classified as sepsis stated in the methods and not merely stating the international Paediatric Sepsis Consensus Conference criteria. SA-AKI is already a form of severe sepsis based on the authors referenced literature. However, the authors' reference of 2005 consensus conference is not current. I find it a bit worrisome that the authors classified AKI stage 1 together with those with no AKI as "AKI negative" (line 13 – 136). This could have significantly influenced any statistical significance being attributed in their findings. Please is there any reference from literature showing that these groups (those with 'no-AKI' and those with 'mild-AKI' [stage 1 AKI]) have similar clinical features, outcomes, and prognosis? This classification contradicts the stated primary outcome in line 145, which states that "the primary outcome was the presence of AKI according to the pRIFLE, pROCK, and KDIGO classifications". It is also at variance with table 2 and other results as well as analysis. Most of the results and analysis were based on summary of table 2 which ideally considered AKI (-) different from AKI (+) comprising of stage 1, 2 and 3.

I would think that the risk factors are the independent variables (predictor variables or explanatory variables) and not necessarily the secondary outcome as stated in line 146.

A PRISMA chart of recruitment protocol may have been more beneficial in supporting the assumed study design.

Reply: I have add the definition of SA-AKI and Sepsis on page 4, line105-106,page 5, line124-126; I misrepresented the grouping of patients and have revised it again(page 6, line151-153); The outcome was modified(page 6, line162-166).

Results

The authors result statement on line 178 to 181 appears not to be very clear. Please can the authors clarify what they meant? Please how was this result statement (line 178/179), "about 53.23% (33/62) of children were diagnosed with AKI", achieved? Also, the higher incidence of AKI in pRIFLE was apparently referred to as 'higher sensitivity'.

Reply: Thirty-three of the 62 children with sepsis were diagnosed with AKI by all three diagnostic criteria. We have modified our comment as advised(see page 7, line199).

• What are the sensitivity and specificity values of pRIFLE, KDIGO, pROCK in identifying SA-AKI diagnosis?

Reply: Sensitivity is the incidence of AKI, and specificity refers to the incidence of AKI(-) people who may be diagnosed as AKI(+).

• What are the positive and negative predictive values of pRIFLE, KDIGO and pROCK for SA-AKI diagnosis?
Prevalence or incidence calculation cannot be translated to sensitivity nor specificity. To have this assertion requires real statistical backing showing the evidence from the data analysis. This may have been an oversight from the authors or lack of adequate statistical analysis.
Reply: We have modified our comment as advised(see page 7, line199; page 11, line318; page 14, line409;)，I did not analyze the positive and negative predictive values of pRIFLE, KDIGO and pROCK for SA-AKI diagnosis.

• Table 2 showed p-values comparisons between.
o pRIFFLE and pROCK,
o pROCK and pRIFFLE, pROCK and KDIGO, but there was no KDIGO and pRIFFLE
Reply: We have modified our comment as advised(Table 2).

• The incidence of pROCK on line 180 is not the same with what was stated on table 2 and 3, as AKI (+) was reported to be 35. I guess that it might have been an oversight though it appears to be consistent.
Reply: We have modified our comment as advised(see page 2, line51; page 7, line198; page 11, line319;).

• Some of the figures/values appear a bit confusing like on Table 3 on "Clinical features of patients with and without AKI using differents diagnostic criteria", most of the percentages for n-values under "ROCK" don't seem to tally.
Reply: We have checked our comment (Table 3).

• There should be consistency when using 'pRIFLE' and 'pROCK' as opposed to 'RIFLE' and 'ROCK' on the result tables.
Reply: We have checked our comment (Table 3).

• For table 5, I would expect that the authors must have done a bivariate analysis first to identify those clinical characteristics that are associated with SA-AKI and then proceed to perform multivariate analysis.
Reply: Bivariate analysis have done in table 3.

• Several independent variables that were statistically significant on table 3 were not reflected in the multivariate logistic regression analysis on table 5. It would be clearer and more convincing if the authors were able to demonstrate the logistic regression by showing the simple logistic regression and multivariate logistic regression simultaneously in a table.
• In my opinion survival analysis graph should ideally reflect SA-AKI and non SA-AKI since the intent is to determine impact of SA-AKI and not just between "patients with and without AKI". Please can the authors explain why it should be otherwise?
Reply: There are many independent variables, so I select those with statistical significance to be listed in Table 5. Survival analysis graph is my mistake of expressing the content. (page 18, linec528-529;)

Discussion

Please what 'incidence rate' and 'standard' is being referred to here on line 272 statement "the incidence rate SA-AKI in this study was slightly higher than this standard"?

Reply: 'incidence rate' is referred to 33/62 patients diagnosed with AKI by all three criteria in this study. 'standard' is referred to incidence reported in the literature.

The statement on sensitivity and specificity (line 297) seems not to be founded based on the available results. I have not seen from the available results were sensitivity and specificity for pRIFLE, KDIGO and pROCK were reported. However, it appears that the authors were interchanging the use of incidence with specificity which is even more evident on line 297 to 300.

Reply: We have modified our comment as advised(see page 11, line318-319,330-335;)

The assertion on line 322 on ALB level is multifactorial rather than just the reason given by authors.

Reply: We have modified our comment as advised(see page 12, line345-346;)

STROBE statement checklist should be reviewed and updated.

• The authors' STROBE statement checklist reported page numbers or line numbers are not tallying.

• There are several sources of bias in retrospective studies. The authors didn't recognise this in the checklist (9).

Reply: We have modified our comment as advised (see strobe statement).

• Absence of UO per hour should be included here in (12c). UO per hour is an integral part of monitoring in critically ill children more especially those with AKI.

Reply: Because more children in our cases used furosemide and the urine volume statistics were incomplete, we did not include them.

Reviewer C

1. Table 3

a. These data are not presented as "median (IQR)". Please unify.

MAP (mmHg), median (IQR)	59.06±10.55	51.33±11.72	**0.023**	58.75±10.01	50.74±11.88	**0.012**	58.00±9.69	49.47±12.2

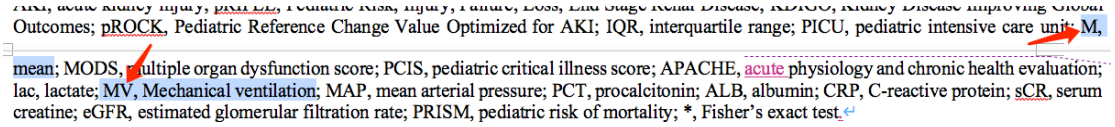
Reply: We have modified our comment as advised (see Table 3).

b. Please also indicate how these data are presented. Please give explanations inside Table.

Relevant scale score			
MODS, [median(IQR]	8.5 [8, 9]	9 [8,12]	
PRISM III score, [median(IQR]	18.0 [14.0, 24]	23.0 [15.75, 31.25]	
PCIS	77.88±10.09	68.98±14.54	
APACHE II	25.81±5.62	28.11±8.01	
Laboratory features [median(IQR)]			

Reply: We have modified our comment as advised (see Table 3).

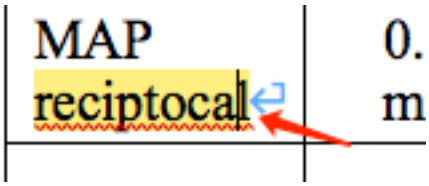
c. No “M, MV” in table 3, but they were explained in table footnote. Please revise.


Outcomes; pROCK, Pediatric Reference Change Value Optimized for AKI; IQR, interquartile range; PICU, pediatric intensive care unit; M, mean; MODS, multiple organ dysfunction score; PCIS, pediatric critical illness score; APACHE, acute physiology and chronic health evaluation; lac, lactate; MV, Mechanical ventilation; MAP, mean arterial pressure; PCT, procalcitonin; ALB, albumin; CRP, C-reactive protein; sCR, serum creatine; eGFR, estimated glomerular filtration rate; PRISM, pediatric risk of mortality; *, Fisher’s exact test.

Reply: We have modified our comment as advised (see Table 3).

2. Table 6

Please check this word.



Reply: We have modified our comment as advised (see Table 6).

3. References

a. References (17 and 19), (15 and 24) are duplicated. Please revise.

17. Ozkaya PY, Taner S, Ersayoğlu I, et al. Sepsis associated acute kidney injury in pediatric intensive care unit. Ther Apher Dial 2023;27:73-82.

19. Ozkaya PY, Taner S, Ersayoğlu I, et al. Sepsis associated acute kidney injury in pediatric intensive care unit. Ther Apher Dial 2023;27:73-82.

15. Wei C, Hongxia G, Hui F, et al. Impact of and risk factors for pediatric acute kidney injury defined by the pROCK criteria in a Chinese PICU population. Pediatr Res 2021;89:1485-91.

24. Wei C, Hongxia G, Hui F, et al. Impact of and risk factors for pediatric acute kidney injury defined by the pROCK criteria in a Chinese PICU population. Pediatr Res 2021;89:1485-91.

Reply: We have modified our comment as advised (see reference, and modify the serial number in the article).

b. Two studies are cited, but ‘A study’ was used in this sentence. Please revise.

A study involving 128 pediatric intensive care units (PICUs) in 26 countries showed that more than half of AKI cases were considered to be closely related to sepsis and were an important cause of death in children (1,2).

Reply: We have modified our comment as advised(see Page3 line 78)

c. The authors mentioned “studies...”, while only one reference was cited. Please revise.

This conclusion is consistent with other related studies (18).

Reply: We have modified our comment as advised (see Page12 line 337, 341,344, 359).

Studies have shown that when MAP <73 mmHg, there is a risk of AKI because it can cause dilation of the afferent arterioles and efferent arterioles of the kidney glomerulus, resulting in a decrease in the

glomerular filtration rate. Even if renal blood flow perfusion is not reduced, renal function can further deteriorate (21).

Reply: We have modified our comment as advised (see Page12 line 356, 359).

some studies have observed that patients who start CRRT within 5 days of admission to the ICU for SA-AKI and within 24 hours of reduced UO have a better prognosis (27).

Reply: We have modified our comment as advised (see Page12 line 356 ,359).