Author’s response to reviews

Title: Epidemiology and outcomes of children with renal failure in the Pediatric ward of a tertiary Hospital in Cameroon

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To the Editorial Office

BMC Pediatrics

Manuscript submission: Epidemiology and outcomes of children with renal failure in the Pediatric ward of a tertiary Hospital in Cameroon

Dear Editor,

Thank you for the opportunity given to address the queries raised by the reviewers during their evaluation of our manuscript referenced above. We are grateful to the reviewers for their time and constructive comments which have been used to improve the manuscript. We have addressed their queries and have used the red color to modify the paper so as to account for their comments and suggestions. All comments to the authors are done in the box as recommended.

We are writing to submit the revised version, hoping that you will find it suitable for publication in your journal.

Yours, Sincerely
On behalf of all co-authors

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Responses to reviewers’ comments

I- Introduction

Comment: Line 30 to 32: Rephrase

Answer: Thanks for the comment; correction done as follow,

“In developing countries the major causes of CKD in children are chronic glomerulonephritis, urologic malformations (posterior urethral valves) and CKD of unknown etiology,”

II- Methods

Comment: DGH: write in full

Answer: Done: “Douala General Hospital”

Comment: This is a retrospective study!!! Was AKI defined by pRIFLE in your center as far back as 2004?? pRIFLE study was published in 2007. You may have to state explicitly how the diagnosis of AKI was made in this retrospective study

Our answer: Thank you very much for this pertinent remark and we agree with you that definition were not clear. We added the following diagnostic criteria in the text:

“AKI was defined using either the modified RIFLE criteria (2004-2007) as an absolute increase or decrease of serum creatinine of at least 1.5 or eGFR of more than 25% from baseline (value on admission) or a reduction in urine output of less than 0.5 ml/kg per hour for more than 6 hours[27] or the Pediatrics RIFLE criteria (2008 -2012), as urine output .05 ml/kg/hour for greater than eight hours and/or an estimated creatinine clearance (eCCl) decrease of at least 25%. If previous eGFR was unavailable a baseline eGFR of 100 ml/min/1.73 m2 was assumed[28].”

“The diagnosis of CKD was based on the estimated glomerular filtration rate (eGFR) lower than 60 ml/min/1.73/ m2, in a patients with either previous abnormal creatinine value and/ or urine abnormalities for more than 3 months, and/or presence of one or more of the following: risk factor for CKD (ex: past history of glomerular disease, urologic malformation) presence of bilateral schrunken kidney, hypocalcemia, hyperphosphoremia [29]

Estimated glomerular filtration rate (eGFR) was determined with the Schwartz formula, using height and serum creatinine (29)”
Comment: Do you mean urine flow rate?

Answer: Yes, Correction done

Comment: State parameters used for this evaluation:

Answer: We have inserted the following:

“For patients with AKI renal recovery (decreased of serum creatinine on admission or increase of eCCl ) was evaluated at 3 months. “

Comment: You need to define chronic glomerulonephritis and PUV diagnosis in this study since they are the major aetiologies and it’s a retrospective study. How were the diagnoses made in those case files?

Answer: Thank you once more for this important remark: we have included definition of these terms as followed:

“Severe malaria was defined as the presence of fever with presence of plasmodium falciparum on peripheral blood film associated with one or more organ dysfunction such as hypotension, coma, need of ventilation, hematologic involvement) and diarrhea as the passage of three or more loose stools per day.

Chronic glomerulonephritis was based either on a past history of a documented glomerular disease and/or the presence of a glomerular syndrome on admission (proteinuria and/or haematuria, hypertension) with bilateral small kidney, decrease glomerular filtration rate, in the absence of identifiable secondary causes.

Diagnosis of posterior urethral valves was made on a past history of documented urology malformation or on ultrasound scan and micturating cystourethrogram recorded.

Comment: Mention these indicators and the definition for their normal value. Remember pRIFLE assumes a baseline CrCL in those without documented premorbid serum creatinine, is this “normal” the assumed CrCL???

Our Answer: thanks once more for this pertinent remark; we mentioned it and the sentence in the text is below:

“Total renal recovery was considered when creatinine or eGFR at 3 months returned to normal or to baseline value for those with CKD. Partial recovery when serum creatinine at 3 months decrease or eGFR increase from the baseline value but did not return to normal and no recovery when at 3 months serum creatinine increase or eGFR decreased compared to admission values.”

Comment: Review this definition of sepsis especially the “suspected” aspect. Is this the protocol in use in your center at the period of study??
Our answer: We have review the Definition (see below) and yes this were the criteria used in our center and still available to date.

“Sepsis was defined as the presence a systemic inflammatory response (fever >38°C, high white cell count at presentation) an increased C-reactive protein level due to suspected or proven infection (by positive culture or tissue stain) caused by any pathogen or a clinical syndrome associated with a high probability of infection[31].

Comment: You mentioned severe malaria as aetiology, this definition should actually be for severe malaria as documented in those case files.

Answer: Thanks a lot: Correction done as below:

“Severe malaria was defined as the presence of fever with presence of plasmodium falciparum on peripheral blood film associated with one or more organ dysfunction such as hypotension, coma, need of ventilation, hematologic involvement

III - RESULTS

Comment: Kindly rewrite the result. It is confusing. No references made to the tables within the result!!! Is that journal recommendation?? Use paragraphs to separate subsections of result: AKI, CKD etc.: 

Our Answer: Thanks very much for the this pertinent remark and we appologise for the mistable, no it is not the journal recommendation and we have includes references of tables in the text and also arranged the results section. but we could not separate AKI and CKD for all variables the result could have been to long with a lot of repetition; hope it could be accepted this way:

“A total of 103 patients’ records (62% males) were included. The median age was 84 months (1QR:15-144). The most frequent clinical symptoms were asthenia (97.8%), anorexia (92.3%) oedema (38.8%) and vomiting (37.8%). In total 68.8% (55/103) of participants were anuric. (table 1).

AKI accounted for 84.5% (n=87) and 86.2% (75/87) were in stage F, with acute tubular necrosis 57.5% (n=50/87) and pre-renal AKI 35.6% (n=31/87) being the most frequent mechanisms. (Table 2) Main etiologies of AKI were sepsis 55.7% (50/83), severe malaria 21.8% (19/87), hypovolémie 16% (14/87) and herbal concoctions 6.9% (6/87), (Table 3).

CKD accounted for 15.6% (n=16) and CKD Stage 5 was the most frequent (81.3%). (table 2). Chronic glomerulonephritis (9/16) and urologic malformations (7/16) mainly posterior urethral valves were the causes of CKD (table 4).

A total of 8 of 14 (57%) with CKD, and 27 of 40 (67.5%) with AKI who required dialysis, accessed it. Reason for non-dialysis were inadapted equipment (57.9%), early death (26.3%),
lack of finances (10.5%) and severe immunodepression (5.3%). Loss to follow up in CKD group was 37.5% (6/16) and in AKI 20.6% (18/87). Of the 25 patients in the AKI group with available data at 3 months, renal recovery was complete in 22 (88%), partial in 1 (4%) and 2 (8%) were dialysis dependant. In-hospital mortality was 50.7% for AKI and 50% for CKD, (Table5). Factors associated to mortality were age <96 months, (p= 0.001), the presence of a coma (p= 0.021), the use of herbal concoction (p=0.024) and the presence of acute pulmonary oedema (p=0.011), (table 6) anuric.(table 1).

Comment: Definition is of utmost importance if reference should be made to this study in future. What is anuria in this study?

Answer: Definition include as follow: “Anuria was defined as urine output less than 1ml/kg/day.”

Comment: Were these sentences referring to the anuria??

Our answer: No this does not refer to anuria; it is a new sentence for the total population.

Comment: Do you mean just infection or sepsis?? Are both interchangeable?? That’s the more reason why you should define what the case files diagnosed as “sepsis”

Answer: Thanks for the pertinent remark: We mean sepsis and correction done and definitions is above

Comment: ???? 6/14 ≠37.5% and why 14 and not 16?? 1/87 ≠20.6%

Answer: sorry it was a mistake; correction done:

“Loss to follow up in CKD group was 37.5% (6/16) and in AKI 20.6% (18/87).”

Comment: Worthwhile to know proportion of them who had dialysis and what form of dialysis

Answer: We mentioned in the results the proportion of patients who had dialysis  (27 out 40), and we added in the methods section that the only RRT available was hemodialysis.

Comment: Why is 96 months the cut off here???

Answer: for pratical reason and for the results to be more clinical we transformed the age in a dichotomic qualitative value and the cut off of 96 months was the value that divided the population in 2 comparable group (57 versus 56)

IV- DISCUSSION

Comment: This first paragraph is another result!!!! Rephrase
Answer: We usually summarize our main results before discussing them, and i really don’t know how to rephrase ;

Comment: This did not stem from this study. No mention was made of duration of symptoms in the result. RPGN can progress to ESRD in a few weeks so presentation at stage 5 disease does not automatically mean late presentation

Answer: Thanks for the pertinent comment and correction done

“Patients were presented with severe disease”

Comment: Not explicit. Do you mean families preference to safeguard the health of a male child??

Answer: Due to financial constraints and cultural believe some families can make such discrimination in SSA

V- TABLE

Thanks for the comments on table and we agree with the comments on table and all the mistake were corrected

Comment: No comparison was done with female gender!!!! Is this preponderance significant??

ANSWER : we did the comparison it and it was not significant

Comment: At what point in the course of the illness was proteinuria documented?? Is this for CKD or both CKD and AKI??

ANSWER: Urine dipstick was done on admission and it was for the total population

Comment : Any documentation on casts??

Answer: thanks, but we did not documented it.

Comment: Does this mean the “acute pulmonary oedema”

Answer: Not necessary : It was dyspnea as symptom but could it could be due to others causes than pulmonary oedema

Comment: Better if degree of dehydration is used to qualify this

Answer: Thanks you for the comment, but we did not record it

Comment: Total is 73 but AKI was 87??????
Answer: Oh sorry for the mistake: correction done

Stages of AKI n (\%)  

<table>
<thead>
<tr>
<th>Stage</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>0</td>
<td>(0)</td>
</tr>
<tr>
<td>I</td>
<td>12</td>
<td>(13.8)</td>
</tr>
<tr>
<td>F</td>
<td>75</td>
<td>(86.2)</td>
</tr>
</tbody>
</table>

Comment: Effectiveness???

Answer: not really we changed it to “dialysis done”

Comment: Inadequacy

Answer: “inadapted”

Comment: ??? Do you mean HIV?? Define please

Answer: Yes, immunodepression was due to HIV and we have insert it in table

Comment: No mention made in the presenting symptoms except dyspnoea

Answer: Thanks for the remark. We also used the symptom in logistic regression but they were not associated to death. we decided to show only factors with significant p value in the table

Strength and Limitation

Comment: It could be made better!!!

Answer: We tried to ameliorate

“Our study has some limitations: This was a retrospective study in which accuracy of data collection can be doubted, also all the shortcoming of such a study design such as the absence standardization in the assessment of variables and the issue of missing data or cases. Also because of lack of diagnosis facilities (renal biopsies, genetic test) some disease may have underestimated in this study.”