Reviewer's report

Title: Prevalence and determinants of chronic kidney disease in rural and urban Cameroonians: A cross-sectional study

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Reviewer: John Stanifer

Reviewer's report:

The authors have posed an important question which is to define the community prevalence of CKD in Cameroon. It has not been well-described before and this work represents an important step forward in defining the epidemiology of CKD in sub-Saharan Africa. Based on this, the work is important and merits dissemination; however, there are a few important points where I think the authors could make their argument/message stronger and many that need clarification.

Major Revisions:

1. In the introduction, the authors claim that CKD is 3-4 times more common in Africans (by virtue of their ethnicity) than in Caucasians. The citation (#3) does not fully support this, and I am not sure that it is accurate. I think what they mean to say is that the prevalence is 3-4x higher in Africa than in high-income countries, but even this is not entirely clear as other works suggest that it approximates the prevalence in high-income countries but there is no strong evidence to say 3-4x times higher.

2. On lines 12-14 (page 3), the authors state that previous work in the region (Central Africa) has been sub-standard and thus are likely inaccurate. They should expand on why they believe this to be the case as two of these citation (by Sumaili, et al) are of high quality with good sampling and use reasonable definitions of CKD. Therefore, the authors need further justification in why the estimates by those works are ‘likely inaccurate’. There is no doubt however that the data in the region are sparse and that more epidemiological studies are needed.

The methods are appropriate for answering the research question, and the authors have been thorough in their design and sampling methods. However, there are a few questions that I have pertaining to them.

3. There is no citation for the region/district level population data; the authors need to cite the National Census or an equivalent source.

4. Under sampling procedures, lines 4-18 (page 4) are quite dense and required multiple readings on my part. A flow diagram would be helpful (though not necessary) here.

5. On line 7 (page 4), I assume that ‘cluster step’ is something similar to sampling
interval (which equals total population/#clusters) which is usually added to a random number between 1 and the sampling interval (in this case 1399) in a repeated fashion until the number of necessary clusters are chosen. This is usually done (as the authors have) from a list of the sampling areas with the population successively added. However, this is not so clearly stated in this section and I think could be much simplified by just stating something like, “we used population proportional to size at the first level to identify the required number of clusters” and all the details about sampling interval, etc could be moved to an appendix. I also will add here as a note - though I do not expect the authors to necessarily respond to it - that the list of health areas listed in the appendix is in alphabetical order which probably does not affect the randomness of it so much, but usually in this technique the list is shuffled around randomly.

6. The authors took such care and thoroughness in describing their first stage of sampling, but seem to move over the next three stages very quickly. At the second level of sampling (village), it is not clear how the villages were randomly chosen. Did the authors have a full list of all villages in each health area? If so, did they use population proportional to size at this level as well? That is, if they did not use population proportional to size and one of the villages has 1000 persons while another has only 100 then the probability of being selected is not the same (thus the randomness is affected) and this would require weighting techniques in the data analysis. The same questions apply for the third level of sampling (neighborhood).

7. At the fourth level (household), the authors do not state how they chose the starting point. Was this based on random geographic points or some other way? It should also be noted that by starting at a market, church, health centre, or school that they will disproportionately select individuals who live close to these and these people may be systematically different than those who live farther away (e.g. they may have a higher socioeconomic standing and thus can afford to live closer to these conveniences). This is fine, but the authors should acknowledge this as a limitation or source of selection bias.

8. One of the most important omissions here in the methods is the non-response rate (this could also be stated in the results instead of the methods but it must be stated somewhere). This could potentially represent one of the biggest sources of bias in the study and must be acknowledged and clearly stated. In addition to the non-response rate, the authors might also state whether they used any techniques to reduce it like second visits, or evening visits, or weekend visits.

9. The data collection procedures are well described for the most part, and they authors have certainly used high quality measurements for CKD which is to their credit. It is especially impressive that they were able to obtain repeat confirmation of renal abnormalities which is of the highest standards. However, I would ask that they elaborate on line 14 (page 5) how the blood pressure was measured. Was this a one-time measurement? Was it an automated or manual sphygmomanometer? Did the participants have adequate time to rest before hand and were the cuff sizes appropriate? These are all important sources of
error in BP measurements.

10. Under definitions and calculations, I have a few comments that I think will make the paper much more readable and understandable. First, the authors use three different formulas to estimate GFR but then mostly end up discussing the MDRD. I would suggest that for the primary analysis/results, they stick with only one estimator (preferably MDRD or CKD-EPI). Then as a secondary analysis they could present the differences that they observed among the three formulas and discuss what these differences may mean.

11. I would also suggest that the authors use more standard nomenclature when discussing CKD, i.e. use the KDOQI or KGIDO staging classifications. The term chronic renal failure (CRF) is odd to me and not typical, and it is especially confusing when discussed alongside chronic kidney disease (CKD). By sticking to the staging, they would avoid these confusing parallels, and it would also make the results more clear. For example, rather than the reader having to figure out how many people overlap between CKD, CRF, and albuminuria, he/she would easily know that if the prevalence of CKD Stage I or II is XX% then those patients by definition have albuminuria without a reduced GFR. The same would go for Stage III, IV, and V. This would also correct a major problem of Table 3 which is the column of ‘Persistent Albuminuria’; the denominator in this column is not correctly specified because not everyone in the sample (439) was tested for persistent albuminuria (only the 85 who returned after the first measurement returned for the second test), but the way that the column is titled would make it suggest that everyone (439) was tested for persistent albuminuria. If the column was titled CKD Stage I/II then the denominator would be correctly specified because everyone in the sample (439) was tested for CKD. This may seem like minor semantics but it speaks to the confusion caused by the authors’ odd disease classifications.

12. My last comment for the methods is from the statistical analysis section. The authors appropriately point out early on that they accounted for the cluster design effect when calculating their sample size, but they do not state whether the accounted for the clustering effect on the variance. That is, the cluster design will increase variance around a point estimate which will increase confidence intervals. Given the 4 stage cluster design used here, I would suggest that they authors try to account for this effect in variance. SPSS software is well-equipped for complex survey analysis and using something like the Taylor series linearization technique would easily do this. This point is not necessarily major but if the authors do not use this in their analysis, then they should at least state it as a limitation especially when it comes to making assumptions about the statistical significance of relationships (that depend on these confidence intervals).

13. Overall, the results appear to be sound.
One major limitation is that confidence intervals are not presented for the point prevalence estimates, e.g. it is very important to know the variance around the final reported prevalence of CKD.
14. It is also a bit confusing to present in detail how many participants had renal abnormalities on the first round of testing and then how many had abnormalities on the second confirmation. If the definition of CKD, as used by the authors, is persistent albuminuria/GFR reduction, then I would simply state what the prevalence of CKD is that they found. This, by definition, would mean that it was persistent. If the authors want to show the readers how many people tested positive in the first round, then a flow diagram might be a clearer way to do so, but otherwise why present (in the authors’ words) a sub-standard definition of CKD?

15. On line 20 (page 7) the authors make mention of awareness and unawareness of disease status; this awareness/unawareness variable should be defined in the methods. I would also suggest to the authors that rather than using awareness of disease status among all participants as an outcome they may want to use awareness of disease status among those who tested positive, i.e. how many people with CKD, diabetes, hypertension were aware that they had it? This would be more valuable because presumably large numbers of any population (Africa or anywhere) are unaware of their disease status because most people do not have disease (I myself am unaware of my status for these diseases). Also during this section the authors make mention of gout, but from what I can tell they did not test for gout. Therefore, the value of asking people whether they think they have gout (awareness of it) when the authors themselves cannot confirm either way seems small.

16. In the results section, the authors also need to be careful not to use the words proteinuria and albuminuria synonymously. For example, on line 1 (page 8) they status albuminuria prevalence is 19.6% but what they mean is dipstick proteinuria (this is important because one is qualitative and the other is semi-quantitative).

17. Also, on line 6 (page 8) they authors state ‘longstanding users of street and herbal medicines’ but what is meant by ‘longstanding’ and what is meant by ‘street medicine’? Are the over-the-counters, traditional medicines, biomedicines, contaminated drugs, illicit drugs?

18. Table 2.

The units in the row labeled ‘Mean serum Creatinine’ do not appear to be right. The mean serum creatinine for the population could not have been 10.6mg/dL as this would be grossly abnormal. Likewise, I do not think that it would have been 10.6 mmol/L either as this would be too low, so I do not know where these units come from but perhaps I am mis-reading the table.

I also do not understand where the numbers come from in the Rows for MDRD, CG, CKD-EPI, and Albuminuria. For example, Table 2 would make it appear that 47 people (10.7%) had an eGFR <60 by MDRD but the authors clearly state in the text (and in Table 3) that the prevalence of ‘chronic renal failure’ was 2.5%. Likewise, the numbers for albuminuria do not match anything in the text. How can 120 participants (27.3%) have albuminuria >30 and eGFR <60 when only
113 (25.7) participants (as stated on lines 13 (page 7) had any renal abnormalities at all on the first screen? For these reasons I cannot figure out how Tables 2 and 3 sync up and Table 2 does not seem supported by the text or the results. The authors needs to clarify themselves on these points.

19. The manuscript does not state what the funding source for this work was.

20. Yes, the discussion and conclusions are adequately supported by the data, but I believe that the authors could dig a little deeper into their findings and they have over-stated their findings in some places (e.g. lines 5-6 on page 10). One place where they could dig deeper is in the rural/urban differences. Why do the authors think that they saw this? The association with herbal medicine use and the other NCDs (diabetes and hypertension) is also very interesting...

21. I also do not think that lines 12-20 (page 10) add much to the discussion. The authors suggest that single time point measurements are inaccurate in estimating eGFR but there could be many factors at play. For example, what about the role of survivor bias? It is certainly the case that people die more frequently (especially when healthcare access is poor) as their GFR falls; therefore, it could be that other studies see difference rates of advanced stage CKD due merely to the fact that healthcare access or death rates are different. Either way, this doesn’t seem to add much as the strength of this paper is in the community-based estimates of CKD in context with other NCDs.

21. The limitations are not clearly stated. The authors do not address non-response bias (or report a non-response rate) nor do they fully address any selection biases in their procedures (e.g. their choice in starting points for random household selections). Further there is no discussion about how their study sample compares to the population at large. For example, how does the study breakdown of men/women; urban/rural; age; etc compare to the expected distribution based on what is known from the census? This would help speak to both selection bias and non-response bias in a strong way. The authors even hint at it on lines 22-23 (page 11), but this could actually be measured or quantified rather than just stated.

22. There are quite a few spelling and grammatical errors that need to be corrected.

Minor Revisions:

1. On lines 5-6 (page 3), the authors should state ‘dual burden of communicable diseases and non-communicable diseases including CKD’.

2. On lines 10-11 (page 3), the authors state that GN, diabetes, htn, HIV, obesity, and herbals are the main contributing causes of CKD in sub-Saharan Africa, but part of their argument is that the epidemiology is not well defined. They would be better to state that these are potentially important etiologies.

3. The study area is well described in lines 18-22 (page 3) but a map or some type of visual aid would be helpful to readers not familiar with the region or
country. This would help readers understand where they are geographically.

4. On line 7 (page 5), as a minor point, the authors state ‘confidence interval of 1.96’ but the confidence interval would really be the mean +/- standard error x 1.96.

5. I would suggest that the inclusion/exclusion criteria on lines 8-10 (page 6) be stated earlier on in the methods; maybe under study design or sampling procedures.

Overall, I think this is a very valuable study and could contribute substantially to the literature. It would be very impactful for both local and global researchers/practitioners, but there are many important points that need clarification. As such, the manuscript is not yet suitable for publication as it stands, and it will require major revision.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:  

I declare that I have no competing interests, and I agree to my signed report being passed on to the authors.