Author's response to reviews

Title: Epidemiology and Risk Factors of Chronic Kidney Disease in India - Results from the SEEK (Screening and Early Evaluation of Kidney Disease) Study

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Author's response to reviews: see over
Dear Editor,

We thank you very much for considering our manuscript and we also thank the reviewers for their important comments. Please see below our point-by-point response to their comments.

**Reviewer's report**  
**Claudine T Jurkovitz**

1) Major compulsory revisions

1.1 The objective of the study is unclear. The authors state (page 4) that the SEEK project was designed and performed to generate data to determine the prevalence and risk factors for CKD in India. However, the prevalence of CKD in the population cannot be assessed from a convenience sample, as recognized by the authors in the discussion. Are the characteristics of the overall sample (n=5,588) similar to the characteristics of the overall population in India (age, gender, prevalence of diabetes, of hypertension?)

Since there are limited studies on the epidemiology of CKD in India, we considered using the convenience sample design was reasonable to start generating such data on prevalence and risk factors of CKD. Regarding the representativeness of our sample as to the Indian population, our study has more hypertension prevalence estimates than was reported in other studies (reference 4 and 5 in the response to review), but it approximates to the general population regarding the other factors.

1.2 What made a person eligible to participate in the screenings? The authors compare the SEEK program to the KEEP program. KEEP specifically targets people at high risk for kidney disease, such as patients with diabetes, hypertension, family history of kidney disease, or family history of diabetes or hypertension. Were the same criteria applied to SEEK? The inclusion/exclusion criteria should be listed in the methods. The objectives of the study would also be clearer if the target population was better defined.

Any Indian male and female with age over 18 years are eligible to participate in the screening. At the time of screening, we didn’t exclude any participant. However, we excluded participants with several criteria that are included in figure 1. Additionally, this statement has been added in the methods section.

“Any Indian male and female with age over 18 years are eligible to participate in the screening”

1.3 The limitations of using a dipstick to estimate proteinuria should be discussed. Proteinuria is generally overestimated when measured using a dipstick method (Am J. Kidney Dis. 58(1): 19-28; 2011)
We agree with the reviewer to bring this important point. We added this statement to the limitations sections:
“The prevalence of CKD might have been overestimated by using the Bayer's multistix 10 which detects urine protein, not albuminuria.”

1.4 The results shown in table 2 are interesting and a brief description of the characteristics associated with CKD would be helpful (Patients with CKD were older, more likely to be male, more likely to have a high school diploma, more likely to be urban, less likely to have a low income, more likely to be overweight or obese, to have diabetes, hypertension and cardiovascular disease than patients without CKD).

This is a very helpful comment. This statement has been added to the results section:

“Patients with CKD were older, more likely to be male, more likely to have a high school diploma, more likely to be urban, less likely to have a low income, more likely to be overweight or obese, to have diabetes, hypertension and cardiovascular disease than patients without CKD”

1.5 Anemia is not a risk factor for CKD but a consequence of CKD. The authors may want to change the expression “Risk factors”, to “Characteristics associated with CKD”.

Although anemia has been described has as a risk factors for chronic kidney disease in several articles, but the wording has been adjusted according to the reviewer comments. (see references 1, 2 and 3 in the response to review)

1.6 In figure 5, the prevalence of each characteristic (hypertension, diabetes etc…) should be shown for both CKD and non-CKD.

We agree with the reviewer. The numbers for non-CKD subjects has been added and plotted into the bar chart.

1.7 The discussion about the CKD prevalence could be shortened (pages 14-15-16). The authors may want to focus on their results, for example trying to explain why patients with CKD seem to be better educated, wealthier and more urban than those without CKD. These are surprising results when compared for example to the KEEP findings. Likewise, the geographic variation is striking and should be discussed. For example why is the prevalence of CKD among the screening participants in Visakhapatnam, Andhra Pradesh is almost 50% (46.8%) while only 152 patients were screened from this site? How can the difference in CKD prevalence between the sites be explained? Is there a selection bias? How were participants recruited?

We agree with the reviewer in this comment. The results were surprising to as well Therefore we are conducting a sub-study in Andhra Pradesh to further study this high CKD prevalence reported in the main SEEK Study.
2) Minor Essential Revisions

2.1. The use of the Spearman correlation as described in table 4 should be included in the statistical method paragraph.

This has been overlooked. We thank the reviewer for bringing this to our attention. This statement has been added to the statistical analysis section:

“We performed spearman correlation analysis to study the relationship between the presence of CKD and multiple covariates. The values of Spearman’s rho and the p-value have been reported.”

2.2. The numbering of the references page 4 should be changed to a more standard numbering system. For example on line 2 “hypertension (3) and (4)” should be changed to “hypertension (3-4)”, on line 8, “renal replacement therapy (7) and (6) and (8)” should be changed to renal replacement therapy (6-8)

Thank you for the note. This has been corrected.

2.3. Page 9, last line: “when there was one or more of your cells…”, should be changed to “when there was one or more cells…”

Thank you for the note. This typo has been corrected.

2.4. Page 10, last line: Albuminuria is part of the definition of CKD. So, it is not surprising that patients without CKD do not have any albuminuria. Please reword the last sentence of page 10 after deleting “versus 0”.

Thank you for the note. This has been corrected as advised.

2.5. Page 11, line 9: Please indicate the figure number at the end of the sentence about CKD prevalence in the different regions.

Thank you for the note. “Figure 4” has been added to this paragraph.

2.6. Page 11, CKD risk factors paragraph: please indicate the table number at the end of the sentence about the correlations.

Thank you for the note. “Table 4” has been added to this paragraph.

2.7. Page 12, please indicate the table number at the end of the paragraph regarding the comparison between the performance of the MDRD and CKD-Epi equations.

Thank you for the note. “Tables 2 and 3” has been added to this paragraph.
2.8. Page 14, 3rd line from the bottom: the prevalence of reduced GFR is stated as being 6.1% whereas it is 5.9% in the results. Likewise, the prevalence of albuminuria is stated as being 11.3% whereas it is 13.7% in the results.

Thank you for the note. This has been corrected.

2.9. Page 15: The sentence beginning with “In a recent evaluation…” and ending with “142 CKD cases” is unclear and should be reworded.

The statement has been rephrased and it is clearer now.

2.10. Page 17, line 4: It is not appropriate to try to extrapolate the prevalence of CKD found in a selected population to the entire population of India. If the targeted population was better defined as suggested above in question 1.2 (for example patients at high risk of kidney disease, or patients with diabetes or with hypertension) then some extrapolation may be possible provided the population prevalence for diabetes or hypertension was known.

We agree with the reviewer and this statement has been deleted.

2.11. Figure 4: Please correct the typos in the title.

Thank you for the note. This has been corrected.
Reviewer's report
Guillermo Garcia Garcia

The high CKD prevalence reported it might be due to a study population bias.

We agree with the reviewer. However, such bias may have been diminished by the large sample size, mix of urban and rural population, varying socioeconomic status as well as education. Also it is important to point out that our population spanned across India which has a considerably large area.

The prevalence of hypertension and diabetes in the study population it's higher than that reported for the general population in India. Additionally, including patients with known kidney disease or proteinuria in the analysis overestimates the prevalence of CKD.

At the time of conception and conduct of the study, this study aimed at estimating the prevalence and risk factors of CKD in India. We excluded patients who reported dialysis or kidney transplantation. We even excluded patients who didn’t answer these two questions or the answers weren’t reported in the case report form. Then we analyzed the dataset to detect CKD patients (eGFR less than 60 ml/min/m2 or proteinuria). We believe that this inclusion/exclusion criteria is reasonable for the study question.

Bayer's multistix 10 detects urine protein, not albumin selectively. However, CKD was defined as the presence of albuminuria > 1+ on dipstick.

We agree with the reviewer to bring this important point. We added this statement to the limitations sections:
“The prevalence of CKD might have been overestimated by using the Bayer's multistix 10 which detects urine protein, not albuminuria.”

Anemia is not a risk factor for CKD; is one of its complications.

Although anemia has been described has as a risk factors for chronic kidney disease in several articles, but the wording has been adjusted according to the reviewer comments. (see references 1, 2 and 3 in the response to review)

Some references are quoted incorrectly: "incidence of diabetes (2) and hypertension (3)and (4)". "only 10% of the Indian ESRD patients receive any renal replacement therapy (RRT) (7) and (6) and (8)"

Thank you for the note. This has been corrected.

There are typing errors in figure 4: "Prevalence of CKD across screening centers"

Thank you for the note. This has been corrected.
Editorial Comments:

1. Authors' Contributions
Please can you remove the Authors' Contributions document from the additional files and include this information after the Competing Interests section in your manuscript.

The authors’ contribution has been included in the manuscript file in the advised place.

2. Tables
Tables should be included in the main manuscript document, and appear after the References and Figures Legends section. Please remove these from the additional files.

The tables have been included in the manuscript file in the advised place, and the figure legends have been added too.

3. Figures
Figure images should be uploaded separately on the submissions page. They should not be included in the main manuscript. Please remove these from the additional files.

Now the figures are in a separate file.

4. General Formatting
Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). Further information regarding the formatting of manuscript can be found here, http://www.biomedcentral.com/bmcnephrol/authors/instructions/researcharticle#formatting-title. It is important that your files are correctly formatted.

The formatting has been reviewed and the author details have been inserted.
References used for the response to review:


