**Author’s response to reviews**

**Title:** Gender-related differences in clinicopathological characteristics and renal outcomes of Chinese patients with IgA nephropathy

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To: BMC Nephrology

Cover letter

Dear Dr. Hayley Henderson,

Thank you very much for your and the reviewer’s comments and suggestions on our manuscript “Gender-related differences in clinicopathological characteristics and renal outcomes of Chinese patients with IgA nephropathy” (BNEP-D-17-00433). Your affirmation on our work has greatly encouraged us to improve our manuscript quality.

We are very appreciative of the reviewer’s comments and suggestions. We have revised the manuscript according to the reviewer’s comments and suggestions and responded the reviewer’s questions point by point as listed below.

I would like to re-submit this revised manuscript to BMC Nephrology, and hope it is acceptable for publication in the journal.

We are looking forward to hearing from you soon.
Sincerely,

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Responses to editor and reviewer’s comments

First of all, we thank editor and reviewer’s positive and constructive comments and suggestions.

1. Response to Helena Zakharova (Reviewer 1)

- The manuscript is quite interesting and deserves publication. However, careful proof reading should be done to correct multiple grammar and style errors. Better to engage native English-language speaker to revise the manuscript. In addition, the abbreviations should be shown in the bottom of each table.

Re: Thanks for the comment. We have carefully revised the manuscript according to your suggestion, including grammar and style. And we have now added abbreviations in the bottom of each table.

- With regards to the content, cohort of patients is mentioned in the discussion several times. However, this is a retrospective study; therefore it is not a cohort in fact, but rather group of patients.

Re: Thanks for pointing it out. This is a retrospective study, male and female groups of Chinese patients with IgA nephropathy were investigated. We have now revised the content accordingly.

- Beyond that, describing outcomes, ESRD or doubling of serum creatinine is indicated. However, it is not clear, whether the authors mean ESRD or doubling of serum creatinine from the time of biopsy to the end of follow-up period, as it is shown in the results, or any other period of time.

Re: Thanks for the comment. And yes, the renal outcomes were collected from the time of biopsy to the end of follow-up period. We have now clarified this information in page 6.

- In addition, discussion contains many repetitions of the same statements, like "We found that male patients presented with worse clinicopathological features", which is repeated at least 3 times within two pages. That might be expressed in
the different way, if needed. And finally, the conclusions postulate, that despite the worse clinical and pathology presentation, males have the same long-term renal survival as females. This paradox should be briefly explained in the end of Conclusions section, otherwise those who will read only the abstract might be confused.

Re: Thanks for the suggestion. We have now revised the discussion and conclusions of the manuscript.

2. Response to Claudia Yuste Lozano (Reviewer 2)

1. I noted that the population is pretty young (mean age 32 years), did the authors excluded old patients? did they have any specific biopsy policy?

Re: Thanks for the comment. We included all patients that age ≥14 years old, without exclusion of old patients. There was no specific biopsy policy for the patients.

2. The paper need a definition of gross haematuria and microhaematuria, as well as clarify the detection method of haematuria/ discrimination of glomerular vs non glomerular haematuria. Have they excluded patients with prior history of kidney stone, urological malignancies or menstruating females? Because haematuria’s prevalence between gender in the current cohort is quite the opposite than the previously described.

Re: Thanks for the suggestion. Episodes of gross hematuria were determined by patient self-reporting. Microscopic hematuria was defined as >3 red blood cells in high field power on microscopic evaluation. We have excluded patients with kidney stone, urological malignancies or menstruating females. Phase-microscope was applied on urine sediment to discriminate hematuria from glomerular or non-glomerular. We have now added the definitions for these clinical parameters in page 6.

3. The follow up seem to be short for a disease that when is not aggressive use to evolve during more than 20 years, especially in young patients with mild presentation. I will suggest that this point should be discussed over the text.

Re: Thanks for the suggestion; This is a retrospective study, with a median follow-up time of 48.6(34.7, 62.7) months. We will continue to follow up these patients. The current follow up time was not long enough compared to the development of the disease, we have now added this limitation in the discussion part in page 13.

4. Combined end-point: each one should be specified in results; how many patients reach each of them? Because is not the same ESRD that doble SCr.

Re: Thanks for the comment. After a median follow-up period of 48.6 (34.7, 62.7) months, 107 (10.8%) patients reached renal outcomes. A total of 16 (1.6%) patients achieved doubling of SCr, and 91(9.2%) patients reached ESRD. We have now added the information in page 9.
5. Although currently there is not guidelines for IgAN therapy, I understand that the author should make an improvement in clarifying the possible bias of the effect of treatment on evolution.

Re: Thanks for pointing it out; The effect of treatment on the progression of IgAN should be considered. But therapeutic regimes were flexible according to physicians’ clinical decision making, and immunosuppression, in particular, was not standardized, so that such unadjusted confounding impairs data interpretation. We have now clarified this possible bias in the discussion in page 16.

6. Very weak and not properly up dated references, for instance author refer a recent meta-analysis one from 2002 (ref 8) with is not specific for IgAN as referred in the text. I kindly suggest reviewing and improving the discussion with up to dated references.

Re: Thanks for the suggestion. We have now updated several references.