**Author’s response to reviews**

**Title:** Rapid decline of renal function in patients with type 2 diabetes with heavy proteinuria : A Report of Three Cases

**Authors:**

CHRISTOPHER LIM (drchrislim@gmail.com)

Nurul Zaynah Nordin (nurulzaynah@gmail.com)

Nor Fadhlina Zakara (fadhsara@gmail.com)

Anim Md Shah (animyss@yahoo.co.uk)

Kalaiselvam Thevandran (kthevandran@gmail.com)

Wan Zul Haikal (wzhaikal@gmail.com)

Bak Leong Goh (bak.leong@gmail.com)

**Version:** 2  **Date:** 08 Nov 2018

**Author’s response to reviews:**

Editor Comments:

In addition to the referee comments, please address the following editorial points:

1. Title: please add ": A Report of Three Cases" to the title. Please make sure the abstracts and title are identical in the submission system and PDF.

   **Answer:** Thank you and this is now added.

2. Case presentation. Please remove the patient initials for all three patients (e.g. Mr NL).

   **Answer:** The initials are removed from the text and table.

3. Consent for publication: this section currently only refers to one patient. Please indicate whether all three patients provided written informed consent for publication.
Answer: All 3 consented and indicated in the written consent.

4. Author Contributions: It is not currently clear that all 6 authors meet the criteria for authorship. Please see: https://www.biomedcentral.com/getpublished/editorial-policies#authorship

Please add details on the clinical role of each author (e.g. management of the patients) in addition to preparing the manuscript. Any authors not meeting the criteria for authorship should instead be mentioned in the Acknowledgements section.

Answer: The required information is added accordingly.

Thank you.

BMC Nephrology operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.

Reviewer reports:

Ravi Nistala (Reviewer 1): This is a manuscript by Lim et al on the matter of rapid unexpected decline in renal function in T2DM patients. While the concept is interesting and may be true to some degree, the presence of interstitial nephritis is a confounding factor. This suggests that most likely there was AKI superimposed on CKD mostly likely due to concomitant infections or antibiotic administration. In addition, the authors brought out the fact that there could be intake of nephrotoxic herbal medications or volume depletion (diuresis or poor oral consumption) or administration of contrast dye for CT scans. I suggest to address these issues in their discussion. Below are some other suggestions which may make the manuscript more readable.

Answer: Thank you and we have made some discussion regarding the possible of other confounding factors that may contribute to the rapid deterioration.
1. There are a lot of lab values and dates that are mentioned one after another with no sequential listing. Please make tables with dates and lab values in columns to identify which lab value corresponds to which date so that the reader can identify a serial decline in creatinine/eGFR. One table can be made for each case. While describing the case, the same should be done. Mention the date of the event/lab and under that describe the lab values, blood pressure etc. Making one table for each case would also mean that the current table is redundant and can be removed.

Answer: We have made the tables with the data.

2. It may be helpful to identify the biopsy pictures with the patient number

Answer: The pictures now are labelled with patient number.

3. If serology was done such as for post-infectious GN, it should be described. There is some mention of serology for one patient. Was serology done for all patients? if yes, and negative, that would add more value to the argument against other GN’s, although interstitial nephritis cannot be refuted.

Answer: Only Madam C has ANA carried out, which was negative. The rest has no serology as there were no features of autoimmune disorders.

Robert C. Stanton (Reviewer 2): The manuscript by Lim et al reports 3 cases of rapid decline in GFR in diabetic patients. As such I have no particular comments on the cases or the discussion. Other than some improvement in word usage I have no suggestions. The main observations are that heavy proteinuria as well as increased blood pressure and uncontrolled diabetes can lead to very rapid decline in GFR. These reports are interesting but rapid decline in GFR due to these causes is reasonably well known to nephrologists. I think this would be more useful to be in a different journal to make general internists aware of the possibility of rapid decline in GFR.

Answer: Thank you for the comments. We wish to have the opportunity to publish this paper in a nephrology journal as the magnitude of GFR declined has far exceeded our normal expectation of a diabetic patient. This can highlight the fact that if DM is poorly controlled, consumption of supplement or traditional medications can be detrimental.
Paul N Epstein, PHD (Reviewer 3): The manuscript concludes that T2D patients with severe proteinuria are at risk of very rapid decline in GFR, possibly related to herbal supplements. The conclusions are from 3 presented cases, all of which are consistent with their conclusions. No control cases are part of the study. The patient findings are clear, the meaning is not. Two of three cases had infections and uncontrolled glycemia, both are potential contributors to the outcome. If possible information on the herbal supplements used by the patients should be added and could be valuable. It would also be useful if the authors indicated whether most other T2D cases in their care with such severe proteinuria had stable renal function. The authors are not trying to make a scientific point, rather they are giving a warning to closely watch T2D patients with nephrotic levels of urine protein for sudden renal decline.

Answer: Thank you for your valuable comments. Some of the supplements consumed are ‘pomegranate juice’ and various unnamed herbal pills and drinks. There were also western supplements such as vitamins. As the patients cannot name the comprehensive list of supplements taken, we had no choice but to omit their names. In our experience, patients who has proteinuria of more than 5 gram day does experience rapid deterioration of renal function, and from casual observation, the higher grade the proteinuria, the faster the renal decline will occur.