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TO THE EDITOR

Name of journal: World Journal of Nephrology

Manuscript NO: 33813

Title: Exercise induced albuminuria and circadian blood pressure abnormalities in type 2 diabetes

Dear Editor,

On behalf of my colleagues, I thank all the reviewers for their careful reading of our manuscript and for their helpful comments and suggestions. We have made changes accordingly and we believe that the result is a greatly improved paper. All the new changes are highlighted in blue in the revised version. Our point-by-point replies to the reviewers and editor are below. We are most grateful for the opportunity to publish in *World Journal of Nephrology* and thank you for your consideration.

Sincerely,

Dr. Jean Jacques N. Noubiap



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Response to reviewer 1

Reviewer's code: 00503339

Reviewer's country: United States

Science editor: Fang-Fang Ji

COMMENTS TO AUTHORS

Well done important information supporting the view that patients regarded as not afflicted with diabetic nephropathy may indeed be progressing towards renal damage that is preventable if treated before diabetic nephropathy progresses to a 24 hour disorder. Further, longer duration studies are to be encouraged.

Authors: Thank you for this appreciation and the suggestion made. We agree with the reviewer that long duration prospective cohort studies should be conducted on the topic as recommended in the discussion



Responses to reviewer 2

Reviewer's code: 00503252

Reviewer's country: Japan

Science editor: Fang-Fang Ji

COMMENTS TO AUTHORS

Tankeu et al. examined whether there was a relationship between resting and exercise-induced albuminuria and circadian variations of BP measured by ABPM in non-hypertensive type 2 diabetes patients. The authors concluded that exercise-induced albuminuria is associated with an increase in nighttime BP values in their patients. Early detection of non-hypertensive type 2 patients with risks for the development of diabetic nephropathy is an important issue, yet there are some concerns in this study.

Major comments

1. Normal control patients should be included. Otherwise you should quote at least references.

Authors: Thank you the comment. Our study was carried out to seek a possible relationship between resting and exercise-induced albuminuria and circadian variations of BP in type 2 diabetes patients. For this purpose, there was no need to have normal control patients.



2. As the authors described in the text, it has been already reported that albuminuria at rest is associated with abnormal patterns of nocturnal BP and that exercise-induced albuminuria has been proposed as a long-term predictive factor of overt diabetic nephropathy. Therefore, this reviewer thinks that it would be necessary to study whether non-hypertensive type 2 diabetes patients presenting exercise-induced albuminuria can improve albuminuria and nocturnal BP values by managing patients. As the authors stated (P11, L3-6), at least the authors should discuss how such patients could be managed meticulously to prevent diabetic nephropathy.

Authors: Thank you for the comment and suggestion. We have accounted for your comments to edit the discussion. However, we would like to notice that our study was as the best of our knowledge the first one investigating the relation between exercise-induced albuminuria and nocturnal blood pressure abnormalities. Therefore, the findings presented here must serve as a basis for studies which will focus on optimal management of non-hypertensive type 2 diabetes patients presenting exercise-induced albuminuria in order to see if this can improve albuminuria and nocturnal BP values in these patients.

Minor 1. 'diastolic BP as well as well as nocturnal MAP (P11.L11)' should be 'diastolic BP as well as nocturnal MAP'.

Authors: Thanks for pointing this out. This has been corrected in the manuscript text.



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Response to reviewer 3

Reviewer's code: 00503180

Reviewer's country: Egypt

Science editor: Fang-Fang Ji

COMMENTS TO AUTHORS



I have some comments for the authors:

1-Authors mentioned that mean age was 52 years, so why did they asked for signature of parents???

Authors: Thank you dear reviewer for pointing this out. This was a drafting error. It has been corrected in the text

2-Please write abbreviations in details before mentioning them.(IQR...)

Authors: Thank You for this suggestion. The manuscript has been revised accordingly.

3-Authors must define the limits of this term (clinical proteinuria) mentioned in the section of methods

Authors: Thanks one more. The term clinical proteinuria refers to an amount of urinary protein ≤ 30 mg/dl. This has been added in the manuscript text.

4-Please to mention the formula of the power of the study in the statistics.

Authors: Thank you dear reviewer for this important remark. The formula has been mentioned and explained in the text accordingly. However, we would like to notice that power of study was set at 90% as indicated and statistics derived used for formula application were obtained from tables presented in reference manuscript.

5-Why did the investigators not measure BP from the right arm as standardized?



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Authors: Thank you for pointing out this issue. BP was measured on the non-dominant arm for ABPM which for our patients was the left arm and the same arm was used for clinical BP measure in order to ensure conformity of measurements and reliable comparison

6-Also authors have to mention the size of cuffs used, how long patients took rest before they measure their BP...more details about the procedure.

Authors: Thank you for rising this point. Participants were maintained in a sitting position for at least five minutes before blood pressure measurement. More details concerning the procedure have been added in the manuscript text as asked

7-Weight must be in kilograms not in cm as mentioned in methods.

Authors: Thanks one again for this remark: This has been corrected in the main text

8-Are there any instructions given to patients before using ABPM devices ?? should be mentioned.

Authors: We thank you for this suggestion. Practical indications on the measurement procedure and the use of the device were explained as well as the constraints related. Patients received instructions concerning the handling of the device and a paper where he/her was thought to notice all particular activity during the day such as medication taken with the hour, any important emotional or physical changing (diary). The detailed procedure of ABPM measurement with instructions has been added in the manuscript



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9-Did the authors excluded patients with proteinuria?? So why did they appear again??

Authors: Thank you dear reviewer for pointing out this issue: Patients with proteinuria were excluded. They did not appear in the analysis but patients with microalbuminuria were not excluded and served for some analysis. Patients included were those with microalbuminuria and not those with proteinuria. But in accordance with the recent recommended terminology, we did not use the term microalbuminuria but rather the term albuminuria

10-Correlation graphs are showing only 24 patients while authors mentioned 27 out of 30 ... and this number is too small to conclude significant results (please to review sample size calculation).

Authors: Thanks one more for this remark. Correlations were first made by the biostatistician only for the first 25 patients. A precision has been included in the revised manuscript to clarify this point.

Please for full revision regarding English grammar.

Thank you dear reviewer for this suggestion. All the manuscript has been modified and revised accordingly.



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