Author’s response to reviews

Title: The Longitudinal Effect of Subclinical Hypothyroidism on Urine Microalbumin-to-Urine Creatinine Ratio in Patients with Type 2 Diabetes Mellitus

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Author’s response to reviews:

Dear Editor and Reviewers:

Thank you for your letter and the reviewers’ comments concerning our manuscript entitled “The Longitudinal Effect of Subclinical Hypothyroidism on Urine Microalbumin-to-Urine Creatinine Ratio in Patients with Type 2 Diabetes Mellitus” (ID: BEND-D-18-00384R1). All these comments are very valuable and helpful for revising and improving our paper. We have studied the comments carefully and made some corrections. The main corrections in the paper and the responses to the reviewer’s comments are as follows:

Reviewer #1:

Comment 1: In the abstract conclusion it states that subclinical hypothyroidism can elevate UACR in patients with type 2 diabetes. It would be more accurate to say that subclinical hypothyroidism is associated with an increase in UACR as the data does not allow conclusions on cause and effect.

Response 1: Thanks to the reviewer for being so rigorous, we have made changes in the abstract conclusion (abstract section, page 2, line 22).
Comment 2: In the methods it is stated that the definition of subclinical hypothyroidism was based on the NEJM definition and a letter is cited to support this. The definition of subclinical hypothyroidism is universally accepted, and I suggest that you define it directly i.e. high TSH concentration and normal FT4 concentration. If you must cite a reference to support the definition then use a major guideline or review paper rather than a letter.

Response 2: Thank you for your suggestion, we have changed the definition of subclinical hypothyroidism to persistently elevated TSH values (at least twice, at least three months apart) with FT4 levels within the reference range, exclusion of previous thyroid disease (Methods section, page 4, line 6-8).

Comment 3: Please cite a recent study which has shown an association between TSH and microalbuminuria in euthyroid individuals with diabetes: Das et al, Ann Clin Biochem. 2019;56:155-162.

Response 3: Thank you for your kind, we have cited that paper (Introduction section, page 3, line 15-16).

Comment 4: Under results, baseline characteristics, it states that there were significant differences in baseline creatinine, e-GFR, TSH, TG and FT3. It would be more useful to summarise here the direction of these differences e.g. patients with SCH had higher creatinine levels, lower e-GFR, higher TSH than euthyroid patients etc.

Response 4: Thank you for your suggestions, we have corrected it (Results section, page 5, line 16-18).

Reviewer #2:

Thank you.
Reviewer #3:

Comment 1: It is better to include the definition of SCH in the main manuscript. "Subclinical hypothyroidism was defined as persistently elevated TSH values (at least twice, at least three months apart) with FT4 levels within the reference range, exclusion of previous thyroid disease."

Response 1: Thank you for your suggestion, we have changed the definition of subclinical hypothyroidism to persistently elevated TSH values (at least twice, at least three months apart) with FT4 levels within the reference range, exclusion of previous thyroid disease (Methods section, page 4, line 6-8).

With kind regards,

Juan Xie