Author’s response to reviews

Title: Age dependent parathormone level and different CKD-MBD treatment practice of dialysed patients in Hungary - results from nationwide clinical audit

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Author’s response to reviews:

Dear Editor,

First of all, we thank again the reviewers for their invaluable help improving the quality of the manuscript. We incorporated the reviewer’s suggestions and revised the manuscript accordingly.

We hope you will find this corrected revision suitable for publication in BMC Nephrology.

Kind regards,

Istvan Kiss

Point-by-point responses to reviewer’s comments:

Reviewer BM:

Major compulsory revisions
One of the main findings of the study is that older patients are less likely to be treated with CKD-MBD related drug therapy. Although not explicitly stated, this might be interpreted as under-treatment of older patients. Instead, it can simply be a reflection of the higher prevalence of older patients meeting MBD-target values and thus a lesser need of therapy in this patient group. The available data
would allow the authors to easily differentiate on this subject. Please elaborate on this.

We do not think that elderly patients were under-treated. In contrast, data suggest that elderly patients met MBD target criteria despite receiving same level of care as younger patients: 19.8% of elderly patients were within target ranges for all parameters (Ca, P and PTH) compared to 15.8% in the younger group. Of the 19.8%, 30.7% did not require treatment whereas this proportion was 18.8% in younger patients. Comparing patients who received versus did not receive treatment in the older group, the proportion of patients meeting target criteria was not different for PTH (53.3% vs 50.4%, p: NS) and P (52.7% vs 52.4%, p: NS). In case of Ca, patients who received treatment were slightly less likely to fall in target range (64.9% vs 69.0%, p<0.05).

Age and diabetic status independently are associated with PTH. Please perform multivariate linear regression analyses exploring the effect of these variables against other relevant variables.

We created multivariable linear regression models with PTH as continuous dependent variable: age (b=-3.61, p<0.001), diabetes (b=-79.76, p<0.001), Ca (b=-145.13, p<0.001) and PO4 (b=165.76, p<0.001) were independent predictors of PTH. In addition, we built logistic regression models with PTH<120 mg/dl as dependent variable: age (10 years increments, OR 1.07 [1.02-1.11], p<0.01), diabetes (OR 1.33 [1.17-1.51], p<0.001), PO4 (0.01mmol/l increments, OR 0.92 [0.91-0.94], p<0.001) and Ca (0.01 mmol/l increments, OR 1.23 [1.19-1.27], p<0.001) were independent predictors of PTH<120. The model also included gender and modality. This latter model was incorporated in the manuscript. In a similar model, age#65 years increased the risk of PTH<120 mg/dl by 33% (OR 1.33 [1.18-1.49], p<0.001).

Minor compulsory revisions

Abstract: <65 and 65+, Please use homogeneous notation
Corrected

Abstract (results). Diabetes (DM) … Diabetes
Corrected

Abstract: Last sentence ‘Drug prescription patterns are greatly influenced by strict rules of medication coverage.’ While this conclusion is valid, the current study does not support this statement.
Deleted

Background: ‘we were going to analyze’ Please rephrase
Rephrased

Patients and methods: I would suggest adding the type of PTH assay used.
The types of PTH assays were added to the text.

Patients and methods: ‘we choose.’ please change to ‘we chose’
Corrected

Results, paragraph 2: The authors state that, although statistically significant, between-group differences of laboratory values are not relevant from a clinical perspective. I agree on this with respect to the serum calcium and phosphate values, but not with the observed lower PTH values in the older patient group, which is one of the main findings of this study. I suggest rephrasing.
Corrected

Results: ‘This unfortunate prescription pattern mirrors the special coverage rules of the Hungarian health insurance’. This statement should be in the discussion section.
The sentence was deleted and it was not moved to Discussion in order to avoid the repetition.

Discussion: Section on hemodialysis vs. peritoneal dialysis patients should be in the results section.
The concerned section was moved into Result section.

Discussion: Please add a sentence on the various PTH assays used to the limitations of the study.
We added a sentence to discussion the limitations regarding the different PTH assays.

Figure 1: >50 needs to be changed in <50
Corrected

Reviewer WQ:
The manuscript certainly reads much better now since it underwent extensive language editing. The information in this manuscript is important mainly to those who work in Hungary but I am still unable to find anything in their study that adds to our knowledge of the CKD-MBD in patients with ESRD in a more general way. The authors can go back and emphasize the parts of their results that they
consider different from what we already know. I believe this is still doable.

We believe that the distinct pattern of CKD-MBD in the elderly, in particular the higher proportion of patients within target ranges despite lesser need of therapy is an important finding in this study. We provided additional supporting data for this concept and we elaborated more on this finding in the discussion.