Author's response to reviews

Title: Novel mutations of PKD genes in Czech population with autosomal dominant polycystic kidney disease

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Author's response to reviews:

Dear Sir/Madam,

Please find revised manuscript “Novel mutations of PKD genes in Czech population with autosomal dominant polycystic kidney disease” as an attachment. We would like to thank to all reviewers for their helpful comments and suggestions. Here we summarize all reviewer’s questions and our responses:

Review by Muhammad Naeem
1. Description of results in abstract section was revised to be more understandable.
2. The sentences “The possible split-site mutations...” (page 6) and “Despite its segregation...” (page 6) in main manuscript were adjusted as reviewer have suggested.
3. The conclusion was corrected.
4. The word affected was uniformly used for patients with ADPKD.

Review by Fiona Karet
1. The data regarding age of end-stage renal disease in set of patients and their affected family members are discussed in section Methods – Patients and also in Discussion, where the correlation between age of ESRD and type of mutation/gender is discussed.
2. As suggested, the explanation of 71% rate of detection by HRM now also includes incorrect original diagnosis.
3. The recommendation regarding addition of segregation of missense alterations in affected families was carried out in Table 5. Segregation rate of small in-frame
Review by Muhammad Hassan

1. As commented, the percentage of ADPKD cases caused by PKD1 or PKD2 is different in clinical identified population and community-based population. The sentence was therefore changed to “In clinical identified populations, mutations of PKD1 gene account...” (page 2). Also, the sentence was moved from Abstract to section Background.

2. Description of results in abstract section was revised to be more understandable (also mentioned by first reviewer).

3. The text was revised to be more reader-friendly as suggested by reviewer.

4. The mention of ethical committee approval was added in section Methods – Patients.

5. The group of patient analysed within this study didn´t include patients from article by Stekrova et al., hence it´s not mentioned in this paper.

6. As reviewer suggested the new section describing linkage analysis was added including list of used markers.

7. A method used for classification of possible pathology of mutation is described in section Methods – Data analysis and sequence changes classification. We used combination of two prediction programs (PolyPhen 2 and SIFT) together with segregation in family. The mutation in Table 1 and 2 are all likely pathogenic mutations (as predicted by mentioned programs), mutations included in Table 3 are all indeterminate.

8. The clinical data of patient were analysed retrospectively, the date about hypertension and renal function were not reliable in all patients. There was only a various description of ultrasound finding. The age of ESRD was the most reliable parameter.

9. Discussion was revised as recommended. The section describing location of mutations in PKD genes was moved in table 1, 2 and 3, instead of special paragraph in Discussion.

Best regards,

Veronika Elisakova