Reviewer's report

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

Version: 1 Date: 2 December 2013

Reviewer: Muhammad Hassan

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Dear Editor

Thank you very much for inviting me to review the original investigation entitled “Novel mutations of PKD genes in Czech population with autosomal dominant polycystic kidney disease” by Elisakova et al.

Elisakova et al presented mutational study on a cohort of 56 unrelated patients with autosomal dominant polycystic kidney disease. Mutation screening of PKD1 and PKD2 genes in these patients resulted in detection of previously reported and novel sequence variations. It is second study in Czech population with large number of patients. Following comments and suggestions will be useful for authors before final acceptance of this manuscript.

Minor Essential Revisions

Abstract: In the sentence “The disease is caused by mutations of PKD1 (approximately 85% of patients) and PKD2 (approximately 14% of patients) genes”, it should be added that this is only for clinically identified populations; community based statistics is different (Ying-Cai Tan et al 2011).

In the sub heading of results, the sentences “Twenty-five of these sequence changes were unique for the Czech population” and “Via the mutational analysis of PKD2 gene, two additional likely pathogenic mutations were detected”, are failed to clarify how many of them are really NOVEL, being unique to Czech population.

Background: Introduction is sound and complete. However, some deletions can be made to make sentence reader friendly e.g. “ADPKD is determined genetically by two genes, PKD1 ([MIM: 601313]; chromosome region 16p13.3) [2] and PKD2 ([MIM: 173910]; chromosome region 4q21-22)”, only MIM number is sufficient.

Major Essential Revisions

Methods: This section needs some essential revisions.

Approval from IRB/ethical committee is not mentioned. A detail of patient phenotype is required; in text or in the form of table. It is important to note that in the previous article by the same group (Stekrova et al 2004), 115 patients with PKD were enrolled and after linkage analysis, PKD2 gene mutations were identified. It is not mentioned that 56 patients presented in this study are same or the new enrollments.
Results: Detail of linkage analysis is not mentioned e.g. which markers were used. Mutation fate is not described. In table 1, an additional column can be added to classify mutations as surely pathogenic/likely pathogenic/neutral etc with the help of Grantham Matrix Score (Rossetti et al, 2007). The used procedure can be added in methods section as well. A detailed Genotype-phenotype correlation is also lacking, especially with reported mutations, one can compare phenotype. For example in patients with large deletions and with two mutations, description of phenotype would definitely benefit us. The authors also mention its need in conclusion “genotyping of PKD genes is important for establishing the diagnosis of ADPKD and evaluation of prognosis of affected individuals”. Comparison of mutation with only mean age is not sufficient. Ying-Cai Tan et al, 2011 may help authors in this regard.

Discussion: Better to start with your own findings very precisely, then compare it with previous studies. This should be done throughout the discussion (lacking at the moment). Better to add location of mutations in tabular form in results. Only then one can discuss under this section. Following sentence is again an example of inappropriate communication, “The potential location of mutations found within this study on the molecule of resulted proteins has been established on the base of theoretical models of polycystins from the UniProtKB/Swiss-Prot database ([Swiss-Prot: P98161] and [Swiss-Prot: Q13563] for polycystin 1 and polycystin 2 respectively)”.

Conclusion: This section is inconclusive, authors described their findings only. A revision is needed.

Figures and Tables: Table 1 should be modified as described above. One figure is not required when so many mutations are described. Better to give figure for large deletion or two mutations present in one patient etc.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'