Reviewer’s report

Title: Determining genomic kinship coefficient seems unhelpful in distinguishing consanguineous couples with a high versus low risk for adverse reproductive outcome

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Reviewer: Hanan Hamamy

Reviewer’s report:

The authors compare the genomic kinship between 73 consanguineous parents having affected children with 78 consanguineous parents with non-affected children. Their results showed that determining the genomic kinship does not help in a more accurate risk estimation for consanguineous couples to have children affected by an AR condition. The title and abstract convey the results adequately.

This is a well written paper that presents an original hypothesis in an attempt to determine a more accurate method for risk estimation for consanguineous couples. The hypothesis is well defined and the methods are appropriate. The authors chose rigorous inclusion criteria to differentiate between their cases and controls. The authors refer to their previous published paper for more details.

Minor comments:
1- In the introduction section, the message in the sentence from line 83 to 86 is not very clear. The authors need to explain in more detail what they mean and to give references if available on predicted number of pathogenic AR variants that can be shared by first cousin couples.

2- The authors compared different parameters between all cases and all controls and at instances, some parameters among the Tunisian population. In view of the ample number of first cousin couples among both cases and controls, it would be interesting also to investigate these parameters comparing first cousin cases with first cousin controls. First cousin couples are the most predominant consanguineous couples who seek genetic counseling.

3- Please give a reference for the sentence in lines 297,298.

4- The authors discuss some reasons for their finding of: “In contrast to our hypothesis, controls show higher point estimates for degree of genomic relatedness” (line 228,229), and in lines 270-272. They could have also compared the R ratio in first cousin couples only with an Rped of 0.125 among both cases and controls and discussed their results.

5- Table S1 can be included as a text table and the authors can minimize the similar description in the text in the methods section.

6- In Tables S1A and S1B, the authors should also include the genomic R for each family.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

No competing interests