OPEN PEER REVIEW

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Shiraz E-Medical Journal
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Peer Review Report for "Intronic Polymorphisms of the Fat Mass and Obesity-Associated (*FTO*) Gene in Association with Morbid Obesity in Southern Iran"

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Review Timeline:

Submit Date: 28 May 2019
Revised Date: 11 Aug 2019
Accepted Date: 14 Aug 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (0) 20 Jul 2019

Dear EIC,
In this study, the authors investigated two SNPs in a small group of morbidly obese patients and healthy controls. There is a number of concerns regarding this study. I recommend a major revision of the manuscript with careful attention to the following points.
1- How significant association between these SNPs and colorectal cancer was measured?
2- Where these two rs1421085 and rs17817449 SNPs are located in the genome? Are they close to any fat metabolism genes?
3- The authors mentioned at least three times, that “to our knowledge, there is still no genetic study…”. I am certain that there is a number of studies around this subject whether in Iran or elsewhere. This repeated claim does not have any base.
4- Study populations are very small without explaining recruitment criteria. The authors should avoid any major conclusions and generalizations of their findings.
5- What are the reported minor allele frequencies of these two SNPs in various populations?
Thanks.

REFEREE: EIC | **Revision (0)** 27 Jul 2019

Dear Author,

The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

“Intronic polymorphisms of the fat mass and obesity-associated (FTO)gene in association with morbid obesity in southern Iran”

ID: 94555

Dear Editor-in-Chief of Shiraz E-Medical Journal

Prof. Kamran B. Lankarani

The authors would like to express their appreciation to the editor and the reviewer for their detailed and professional manuscript assessment. All of the reviewers’ comments were considered and the manuscript has been revised accordingly. The responses of the specific comments of the reviewer are listed in this letter. Revisions in the text are shown using yellow highlights for modifications.

We are looking forward to hearing from you. Thank you very much for your cooperation.

Response to the Reviewer

Dear reviewer

First, we would like to thank you for your useful comments/suggestions on this manuscript.

1. How significant association between these SNPs and colorectal cancer was measured?

"Thank you for pointing this blunder out to us. In this study our patients were morbidly obese patients, not colorectal cancer patients and the manuscript has been revised accordingly. Chi-square test in the SPSS software was applied for evaluation of the potential association between two *FTO* SNPs and morbid obesity. As mentioned in the manuscript (Table 2), the frequencies of these SNPs showed significant differences between morbidly obese patients and normal controls"

2. Where these two rs1421085 and rs17817449 SNPs are located in the genome? Are they close to any fat metabolism genes?

"Thank you for reminding this point. Both of these SNPs (rs1421085 and rs17817449) are located in the first intron of the Fat mass and obesity-associated (*FTO*) gene on the chromosome 16. It has been shown that *FTO* gene is correlated with obesity in humans. The location of these SNPs has been included in the revised manuscript"

3. The authors mentioned at least three times, that "to our knowledge there is still no genetic study…". I am certain that there are number of studies around this subject whether in Iran or elsewhere. This repeated claim does not have any base.

"Thank you for pointing this out. Although there are some related studies on other polymorphisms in Iran, no study specifically investigates the association of two SNPs (rs1421085 and rs17817449) with morbid obesity. Therefore, according to your beneficial comment the sentences have been revised for better clarity in the manuscript."

4. Study populations is very small without explaining recruitment criteria. The authors should avoid any major conclusion and generalization of their findings.

"Thank you for your beneficial suggestion. We agree with you and the discussion part has been revised, accordingly."

5. What are the reported minor allele frequencies of these two SNPs in various populations?

"In the study by Price et al. (Ref 23) the minor allele frequencies (MAFs) were 0.5 for both rs1421085 and rs17817449 in a non-Hispanic Caucasians population. In another study by Do et al. in a French-Canadian population, MAFs were 0.41 and 0.39 for rs1421085 and rs17817449, respectively (Ref 24). Villalobos-Comparán performed similar study in a Mexican population and obtained MAFs of 0.2 and 0.21 for rs1421085 and rs17817449, respectively (Ref 22)."

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Revision (1)

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REFEREE: EIC | **Revision (1)** 14 Aug 2019

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.