Reviewer's report

Title: Hepcidin gene polymorphisms and iron overload in β-thalassemia major patients refractory to iron chelating therapy

Version: 0 Date: 11 Jun 2019

Reviewer: Maria Sonati

Reviewer's report:

The manuscript is interesting, deals with a relevant theme and deserves publication. However, it needs to be better organized, written and, while it may be more concise, it needs to complement information and better discuss the results obtained.

The Abstract should inform how many and who the patients are and what methods were used, as well as to bring a more substantial conclusion: what is the contribution of this work? What is its relevance? What new knowledge is being presented here? Moreover, the choice of the three polymorphisms studied should be justified. Why these and not others? The Results need to be clearer.

The Introduction may be more concise, especially its first paragraph, and again must contain the reason for the choice of polymorphisms. Has this study been preceded by similar ones or is it unprecedented in this population? If there have been previous studies, what is the reason for repeating them? It would also be interesting to characterize beta thalassemia in Iran: what are the most frequent mutations in the country and which genotypes are most common among patients with thalassemia major? Why is this hemoglobinopathy so prevalent in this region? Please, explain.

In Patients, iron chelating therapy should be specified, as well as, if possible, patient genotypes. In Methods, determination of serum ferritin levels as well as iron concentration in the heart and liver should be included.
Each result needs to be better discussed and compared to results from previous studies, in this one, if any, and in other populations. The similarities and differences should be emphasized and explained. Alleles should be classified wild type and mutant. In Table 1 there are no units; in Table 2 there is no information if the alleles/genotypes are in agreement with the Hardy-Weinberg equilibrium: it seems to us that they are not ... if this is true, they are under selective pressure, which also needs explanation.

The Discussion could be more concise and focused on the results obtained. They need to be discussed in more depth. What is the meaning and consequences of the association found? Will the detection of the polymorphism modify the clinical management of the patients? In what way?

The Conclusion also needs to be deepened and focused on the contribution of the study and the new information produced.

English needs revision by a native English speaker.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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