Reviewer’s report

Title: Overtime trend of thyroid hormones and thyroid autoimmunity and ovarian reserve: A longitudinal population study with a 12-year follow up.

Version: 0 Date: 24 Dec 2018

Reviewer: David Unuane

Reviewer's report:

This longitudinal observational study with a 12 year follows up aims to observe and compare the overtime evolution of thyroid function parameters and anti-TPO status in fertile women with different ovarian reserve status. Between groups comparison is performed according to different subgroups of ovarian reserve as indicated by age specific quartiles of AMH.

The present manuscript raises some major concerns:

* General remarks:

1) There are several grammatical errors which makes it difficult to read and comprehend the manuscript especially in the discussion section. This would need some thorough revision.

2) The discussion section is too long, very often out of scope and lacking structure. There is need for downsizing, concentrating on the major aspects of the manuscript and avoiding repetition.

* Introduction:

1) Line 57: I would replace thyroid "disease "by thyroid "dysfunction ".

2) Line 66: I would refrain from using the term "interaction" as it implies some causal relation. I would rather use "any relation". The same comment can be applied for line 220 (discussion).

* Methods:

1) Were the patients interviewed and examined again at follow up visits or only at the entry of the study?
2) At baseline some of the included patients showed to have some degree of thyroid dysfunction (table 2). Were these patients then excluded from the study as probably some would have needed treatment with levothyroxine or anti-thyroid drug?

3) Line: 83: please use levothyroxine instead of thyroxin

4) Line 138: TPO > 35IU/L/ml was considered as TPOab positivity. Is this cut off based on a reference population in Iran (or comparable reference population) were this study was conducted?

* Discussion:

1. Line 228: although in the study by Monteleone et al for the first time the presence of thyroid antibodies in ovarian follicular fluid was demonstrated also found a significantly lower oocyte fertilization and percentage of grade A embryos when comparing infertile women undergoing IVF with thyroid autoimmunity to negative controls. However any pathophysiological mechanism is purely speculative. This should be made clear in the manuscript.

2. Line 232: The authors state that "A study conducted among infertile women seeking gonadotropin treatment, revealed that TPOAb positive women, compared to negative ones, have a poorer ovarian response to gonadotropins referring to the study by Monteleone et al. However in this study I cannot find any data on response to gonadotropins.

3. Line 241: the author's referred to heterogeneity between studies to explain the controversial results. Could the authors explain as to what exactly is meant by this?

**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.

Yes

**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

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal