Author’s response to reviews

Title: The impact of thyroid-stimulating hormone levels in euthyroid women on intrauterine insemination outcome

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Dear Editor,

Thank you very much for your consideration of our manuscript and request for a revised version. We would also like to thank referee for (BMWH-D-17-00439) entitled, “The impact of thyroid-stimulating hormone levels in euthyroid women on intrauterine insemination outcome’ for publication in ‘BMC Women’s Health’. Based the comments from the referee, we have made changes of the manuscript, which are detailed below, and address each one individually.

Reviewers’ comments:

Reviewer 1.

The present work is interesting but to be published it must undergo a thorough revision process.

1. In the introduction, the justification for the study focuses on the impact that subclinical hypothyroidism has on perinatal outcomes. In addition, the authors report the lack of agreement
on the TSH cut-off point to consider that there is a subclinical hypothyroidism. It is evident that the Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum published in 2017 have not been taken into account.

Currently, the cut-off point to consider that there is a subclinical hypothyroidism has gone from 2.5 to 4 mIU/ml. It is necessary to rewrite the introduction including the current criteria of the ATA.

Respond: We added the current criteria of American Thyroid Association in Introduction.


2. In the study period, the accepted cut-off point for subclinical hypothyroidism was 2.5 U/L. Therefore, we can understand that in the study group (TSH≥ 2.5 U / L), if the woman became pregnant, she was diagnosed with subclinical hypothyroidism (We do not know the level of fT4 as it is exposed in the section of limitations of the study). The authors should clarify whether this group of pregnant women was treated with levothyroxine or not.

Respond: We did not give any Levo-thyroxine treatment in the study group.

3. I understand that TSH was determined before initiating ovarian stimulation. However, this point must be clearly expressed in the text.

Respond: Yes, TSH was determined before initiating ovarian stimulation. We added one sentence in Materials- Methods.

4.- Authors should explain how they calculated the sample size. In the case that, as it seems, the authors included the sample universe, it is necessary to clarify the power of the study, specifically in the multivariate logistic regression analysis.
Respond: We added sample size and power analysis in Methods (Statistically Methods)

5.- In the section of methods, the authors include BMI as an independent variable of multiple logistic regression. However, this variable is not included in the results section. It is necessary to clarify why this variable was eliminated or include its result.

Respond: We are sorry for this mistake. We added the adjusted OR for BMI in Result.

6.- The authors state that 38 pregnancies were achieved. However, only the perinatal results of 27 are reflected. It is necessary to explain what happened in the 11 cases in which the gestational period was not completed. It is very important to clarify how many reproductive losses occurred in each group by specifying the number of miscarriages of the first trimester, late abortions and intrauterine fetal deaths were recorded.

Respond: We added the obstetrics results of 11 cases in Table 4.

7. In the discussion, the authors state that the American Thyroid Association believes that preconception point cut and the first trimester of pregnancy to diagnose and treat subclinical hypothyroidism is set to 2.5 IU / L. This statement is not updated according to the latest ATA guideline of 2017 that sets the cut-off point at 4 U / L. The authors must update this aspect.

Respond: We rewrite this section according to 2017 guidelines of ATA.

8.- It would be interesting to include in the discussion a paragraph in which it is reflected that the results found by the authors are relevant since they endorse the recommendation of the 2017 ATA.

Respond: We added a paragraph in Discussion section.

Reviewer 2.

Congratulations on your interesting manuscript. I have some minor recommendations.

Respond: Yes, it is standard protocol. Owing to randomized controlled studies have been shown that controlled ovarian stimulation in combination with IUI has been shown to result in significantly higher cumulative pregnancy rates per couple as compared to unstimulated intracervical insemination, COS alone or IUI alone (1,2), we used the combined therapy for the couples of infertility. We added one sentence in Methods.


2. (Page 5. Line 44) Only husband’s sperm no unmarried couples?

   Respond: Fresh husband’s sperm were used for IUI protocol, because, only couples with a marriage certificate could be start infertility treatment in our country and we enrolled only couples with a marriage certificate in this study.

3. (Page 7. Line 35). No statistical difference, reads as if there were less smokers in the high TSH group, but there is no difference.

   Respond: A total of 29/233 (12.4%) women in the low-TSH group smoked cigarettes, whereas only 5/69 (7.2%) women smoked in the high-TSH group. Although there was higher women smoke cigarette in low-TSH group than high-TSH group, there was no statistically significant difference (p = 0.23) We added a sentence in Result.

4. (Page 7. Line 37). No statistical difference in sperm-quality parameters, but TPMS has a p value of 0.06.

   Needs to be discussed in discussion.

   Respond: We added a sentence about sperm-quality parameter.
Respond: We corrected as requested.

6. Figure. Poor quality
Information between brackets can not be read.
Respond: We corrected the Figure 1 and we improved the quality of Figure 1

Yours sincerely,

Gorkem TUNCAY MD