Author’s response to reviews

Title: Anogenital distance is related to ovarian follicular number in young Spanish women: a cross-sectional study.

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Author’s response to reviews:

Murcia, December 3rd 2012

Dear Editors in-chief,

Ref: Ms. 1043831318419378 - “Anogenital distance is related to ovarian follicular number in young Spanish women: a cross-sectional study”.

First of all, we would like to thank the thoughtful and useful comments and suggestions that we believed have been addressed in the current form of the manuscript.

The revised copy of the document is submitted with all the changes tracked or highlighted in order to facilitate review. As requested, and in order to facilitate the review, we address specific reviewers’ comments point by point in the attached document. A detailed explanation of all the changes introduced in the paper is also provided.

Please, do not hesitate to contact me for any further clarifications that you, the Associate Editor or the Reviewers may find appropriate.

Looking forward to hear from you,

Yours Sincerely

Jaime Mendiola

AUTHORS RESPONSE TO THE REVIEWERS AND EDITORS

Ref: Ms. 1043831318419378 - “Anogenital distance is related to ovarian follicular number in young Spanish women: a cross-sectional study”.
Reviewer's report:

We thank Referee #2 for his suggestions to which we have responded.

Minor essential revisions:

1. Line 107 - the authors should add a sentence summarizing the clinical importance of 6 or more follicles per ovary.

Response:
Following the suggestion of the Reviewer, a sentence summarizing the clinical importance of 6 or more follicles per ovary has been now added to the revised manuscript.

“Having 6 or more follicles has been associated with hyperprolactinaemia, hypothalamic anovulation or weight-related amenorrhoea and may result from incomplete pulsatile gonadotrophin (GnRH) stimulation of ovarian follicular development (29). It may also indicate an ovarian dysfunction in female adolescents with cystic fibrosis (30) or the presence of polycystic ovary (30).”

2. Line 222 the authors should include a discussion on reproducibility of transvaginal ultrasound measurements of follicle number. How reproducible is this?

Response:
Following the suggestion of the Reviewer, a new paragraph on reproducibility of transvaginal ultrasound measurements of follicle number has been now added to the revised manuscript.

“With regard to reproducibility of follicle count estimated by transvaginal ultrasound, it has been shown that determination of follicle count by transvaginal ultrasound results in acceptable intra- and inter- observer variability (40). While there is undoubtedly some inter-cycle variability of follicle count, it is considered to be of little clinical significance, for example, in predicting the response in in vitro fertilization (41).

The following two references have been added to the reference section in the revised manuscript.


Discretionary revisions:
1. The last sentence in the conclusion may overstate the author's finding of an association with AGD and multiple follicles. We don't know that AGD is a stable finding in humans throughout their lives (though it is reasonable to assume so) and, as such, that this phenotypic finding is reflective of prenatal influences.

Response:
The last sentence in the conclusion has been modified in the revised manuscript.

"Therefore, both greater follicular recruitment and longer AGD in adulthood - assuming that AGD is a stable finding in humans throughout their lives - may reflect a common origin in utero, resulting in alterations of the developing female reproductive tract."

Reviewer's report:
We thank Referee #1 for his suggestions to which we have responded.

1. I think the second sentence in the Abstract starting with “Some endocrine-disrupting chemicals…” should be omitted. The present study did not take EDCs into account at all.

Response:
That sentence has been omitted.

2. The authors give a correlation coefficient between the two AGD measurements (r=0.40). I think it would be of interest to see a scatterplot including these measurements.

Response:
Following the suggestion of the Reviewer, a scatterplot including the two AGD measurements has been now added as Figure 3 (Correlations between AGDAF and AGDAC measures in the MYWS).

3. I think the authors in the Results should write “were more likely to have #6 ovarian follicles compared to < 6 follicles (OR 3.0, 95% CI 1.1, 8.6)”, instead of writing “3.0-times … more likely…”.

Response:
That sentence has been modified accordingly.

“. . .were more likely to have # 6 ovarian follicles compared to < 6 follicles (Odds ratio: 3.0, 95% CI 1.1, 8.6)."

4. I think it would add important information to the readers if the authors also give the r2 values (the explained proportion of the variation) in the regression analyses. It will help the readers to evaluate whether both AGD measures, as stated by the author in the beginning of the Discussion, were “strongly associated with the presence of greater ovarian follicular number”. 
Response:
The information on R2 values has been now added to table 3.

EDITORS:
It is important that your files are correctly formatted.

Response:
Thank you very much. The format of the manuscript has been changed accordingly.