**Reviewer’s report**

**Title:** Adrenarche and Pubarche in Girls with Turner Syndrome during Growth-Promoting Therapy with Human Growth Hormone

**Version:** 0  **Date:** 17 Nov 2018

**Reviewer:** Tommaso Aversa

**Reviewer's report:**

This is a retrospective study performed in one single center and reporting data on adrenarche and pubarche in TS patients.

This aspect has been already studied several years ago in a pediatric population with TS, as also reported by authors, and in my opinion this paper does not add any novel information on this topic. However, a different aspect of this paper is that this cohort of TS patients is on GH treatment.

**Major points**

1) Reading the article, I found the presentation of the data quite messy. This is a crucial aspect because data in a paper need to be clearly presented. For example, I did not find in the text if this is a cross sectional or a longitudinal retrospective study.

2) Authors reported that "The cohort consisted of 94 girls and young women with TS aged between 3.1 years and 23.2 years under treatment with human growth hormone (GH) who regularly presented at our outpatient clinic every 4 to 6 months". This sounds to me as a cross-sectional study and as patients were still on GH at 23.2 years of age. Is it correct?

3) Authors reported that they excluded 3 patients from the analysis because "Assessment of pubertal stage was not yet possible in three girls at the time of analysis for reasons of age". What does it mean?

4) Authors should give into the text a definition of adrenarche and report the exact age in which adrenarche occurs

5) Authors should report data on FSH and LH levels at least at Tanner stage 2.

6) Although the age range of patients was 3.1-23.2 years, in results section and in figure 1 data are presented only until 17 years of age.
7) Authors performed statistical analysis with parametric tests, probably assuming the normal distribution of data. However, I believe that DHEAS levels are not normally distributed and therefore authors should verify the distribution and in case of non-normally distributed data they have to perform non parametric tests as Kruskall-Wallis or Mann-Whitney.

8) Figure 1 have to report the significant differences between groups.

9) Table 1 should be remodeled in order to report significant differences between the two groups at the different Tanner stages.

10) Authors report conclusions only into the abstract and they do not seem to be concordant with the reported results. Indeed, Authors wrote "The onset of adrenarche in the girls with TS does not differ from that in healthy girls" but age at onset of menarche is not specified into the text.

Minor points

1) Bibliography have to be in order of presentation into the text and not in alphabetic order.

2) English language should be improved.

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
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