Manuscript Title: Delayed Puberty In Girls With Primary Amenorrhea: A Report of Cases

**Journal of Biomedicine and Translational Research (JBTR)**

Dear Editors

**Journal of Biomedicine and Translational Research (JBTR)**

Thank you for inviting us to submit a revised draft of our manuscript entitled, Delayed Puberty In Girls With Primary Amenorrhea: A Report of Cases to **Journal of Biomedicine and Translational Research (JBTR)**. We also appreciate the time and effort you and each of the reviewers have dedicated to providing insightful feedback on ways to strengthen our paper. With great pleasure we resubmit our article for further consideration. We have incorporated changes that reflect the detailed suggestions you have graciously provided. To facilitate our revisions, the following is a point-by-point response to the questions and comments delivered in review result.

We have incorporated your feedback and hope that these revisions satisfy you to accept our submission.

**Sincerely,**

Fatinah Shahab (First author)

Sultana MH Faradz (Corresponding author)

**Reviewers' and Editorial comments:**

Editorial review:

In general, this manuscript has followed our guidelines. However, some corrections should be made:

1. Please provide running title

2. Please check the co-authors how their names are written.

3. Please provide Acknowledgement part

4. Please check the References again, because some parts are not consistent. Please make sure that they are following our journal’s guideline. (<https://ejournal2.undip.ac.id/index.php/jbtr/about/submissions#authorGuidelines>)

Please change the similar sentences that are highlighted (see the attachment)

**RESPONSE:**

* *Thank you so much for providing these insights.*
* *We have rewritten the co-authors name according to your suggestions.*
* *We agree with you, and we have including an acknowledgment part in this article.*
* *We have now followed the journal guideline for references.*

**Reviewers' comments:**

**Reviewer 2**

Reviewer 2

1. General Comment: good
2. Abstract:

The objective of the study is not clear, is it looking for a relationship between phenotype and genotype, what is the purpose of showing 2 different cases etc.

1. Methodology: hormone examination and ultrasound are still lacking
2. Discussion: there are some interesting things that are not discussed
3. Bibliography/References: good

Recommendation: Requires minor revision

**RESPONSE:**

* *Thank you for your suggestion.* *We thank the reviewer for the comments.*
* *The objective of the study is showing that both cases may present with the same chief complain of delayed puberty (A1M1P1) with primary amenorrhea eventhough the two cases have different diagnosis. The pathogenesis of delayed puberty encompasses several conditions so it is very important to run cytogenetic analysis in patient with delayed puberty with primary amenorrhea. However, the phenotype of delayed puberty in cases which is associated with sex chromosomal disorder may present in several conditions.*
* *You have raised an important point about hormonal examination, unfortunately we cannot provide for another additional hormonal examination for these cases.*
* *We agree that ultrasound is important for both cases and we have mention the result of ultrasound examination for both cases which showed hypoplasia of uterus and ovaries on pelvic imaging in page 4 line 10 for first case and in page 6 line 3 for second case. We did not put the imaging picture in this article because of too many pictures will include in this article.*
* *In our revisions, we have reflected some interesting about these two cases by adding more explanation in discussion and hope that the reviewer will now agree that the article is much improved.*

Reviewer 3

Section I: Comments per Section of Manuscript

1. General Comment:

The two cases of delayed puberty in girls with primary amenorrhea

1. Abstract:

In the (abstract) background, there are still disconnections between sentences, could the author improve the abstract so that the sentences can be more connected?

1. Discussion:

1. Since it is already known that underlying causes of primary amenorrhea can lead to delayed or stalled puberty, or normal pubertal development with no menarche, could the authors please emphasize the originality of this study?

2. The authors reported that the first case had low estrogen levels, whereas the second case had normal estrogen levels. Can the authors elaborate on this result, especially in the context of delayed puberty of both cases despite of different estrogen finding?

1. Conclusion:

There is a discrepancy between the conclusion and the title. The author emphasizes delayed puberty in primary amenorrhea on the title, but cytogenetics is highlighted in the conclusion. Is it possible for the authors to improve the conclusion?

Recommendation: Requires minor correction

**RESPONSE:**

* *Thank you for providing these insights.*
* *We thank the reviewer for the comments, however in background there have been*

*connections between sentences and we have briefly mention about several things*

*associated with puberty.*

* *We have reflected some interesting about these two cases by adding more explanation in discussion and hope that the reviewer will now agree that the article is much improved.*
* *We have clarified that underlying causes of primary amenorrhea can lead to delayed or stalled puberty, or normal pubertal development with no menarche, the originality of this study is about finding the right diagnosis so physicians can make a correct intervention and treatment.*
* *The first case had low estrogen levels, whereas the second case had normal estrogen levels. Delayed puberty can showed normal or low level of FSH according to the etiology, we have showed the correlation between level of FSH and delayed puberty in page 8 on second paragraph.*
* *According to the suggestions and comments of the reviewer we have rewritten conclusion by adding more* highlighted *about delayed puberty and we hope that the edited section clarifies the connection of the title and the conclusion to be more in line and we hope the reviewer will now agree that the article is much improved.*

**CONCLUDING REMARKS**: *Again, thank you for giving us the opportunity to strengthen our manuscript with your valuable comments and queries.*