OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
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- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "Accuracy of Urinary Etiocholanolone/Androsterone Ratio as Alternative to Serum Testosterone/Dihydrotestosterone Ratio for Diagnosis of 5 Alpha-reductase Type 2 Deficiency Patients and Carriers in Indonesia"

Author(s): Nanis Sacharina Marzuki, Firman Pratama Idris, Hannie Kartapradja, Shirley Renata, Alida Harahap, Jose Rizal Latief Batubara

Review Timeline:

Submit Date:	21 Sep 2020
Revised Date:	3 Feb 2021
Accepted Date:	10 Mar 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Samaneh Hosseinzadeh: Reviewer | Revision (0) 14 Oct 2020

Dear AE,
Comments for the authors:
Structural comments
• The main purpose of this article is to evaluate the feasibility of replacing the Et/An ratio instead of T/DHTratio in diagnosing 5ARD2 patients and carriers; However, there is no clear explanation about the role of the Et/An ratio in this deficiency. Also, there is no reason other than the cost for this offer. It is better to add supplementary explanations in this regard to the introduction.
• Information needs to show the ethical approval of the research.
Technical comments
• According to the authors' previous research, which is also mentioned in this article (i.e. ref. 18), the article has no innovation aspect and can be presented as a report or short letter. Otherwise, please specify the new aspects of the article.
• Some data seems to be missed on methods and results and we just encountered them in

tables or discussion. For example:
- Determining the clinical phenotypic effect of the external genitalia with the external genitalia masculinization scores (EMS), which is not mentioned in the text but can be seen in the table.
- In the introduction and methods section, the type of amino acid mutations in steroid 5-alpha-reductase2)SRD5A2(and its role in pathogenicity were not discussed, but in the discussion section, it is mentioned without prior explanation.
- There is no explanation in the manuscript about the reason for the importance of marriage mentioned in the table.
• Participants and their details are not mentioned in the method.
• It is better to briefly mention the technical methods, even though they are according to conventional or reference methods.
• In comparison between Tables 1 and 2, there is not a significant change in the Et/An ratio between patients and carriers groups (1.19 Vs 1.28). Given the focus on the ratio mentioned as an indicator of disease diagnosis, how do you justify this?
• Reading the manuscript title, it seems that the authors' goal is simply to compare the two ratios in diagnosing the disease. But in the text, the main goal is the feasibility of replacing the two ratio. If this interpretation is correct, it is better to change the title.
Thanks

REFEREE: Reviewer | **Revision** (0) 5 Nov 2020

Dear AE,
Comments for the authors:
1- It is necessary to match the keywords with MeSH terms.
2- It is necessary to specify inclusion/exclusion criteria in methods in population studies.
3- Please mention the company name of the kits used in the methods.
4- Please explain the technical methods briefly in the method section.
5- It is necessary to check punctuations and use them correctly.
6- Some sentences in the manuscript need to be grammatically corrected.
7- The information about the ethical approval of the research needs to be shown in the article.
8- What is your background reasons to use the Et/An ratio instead of T/DHTratio in diagnosing 5ARD2 patients and carriers? It is necessary to mention the leading causes of the Et/An ratio in the introduction.
9- In tables, there is some information about the marriage of the patients. If it is an influential factor, please mention how it affects the patients and carriers? If it is not an influential factor, the data about marriage is extra data listed in the table.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 11 Dec 2020

Dear EIC,
The authors should address the reviewers' comments.
Thanks.

Fereidoun Azizi & Dr. Azita Zadeh-Vakili: EIC | **Revision** (0) 13 Dec 2020

Dear Author,

The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Replies to Reviewers

We would like to thank the reviewers for the suggestions and comments

Reviewers 1

1. *It is necessary to match the keywords with MeSH terms.*
   Response: the keywords has been updated accordingly (line 40 – 41)

2. *It is necessary to specify inclusion/exclusion criteria in methods in population studies.*
   Response: the inclusion/exclusion criteria has been specified in methods as suggested (line 103 – 108)

3. *Please mention the company name of the kits used in methods*
4. *Please explain the technical methods briefly in the method section.*
   Response: the methods of hormonal analysis has been revised accordingly (line 138 – 147)

5. *It is necessary to check punctuations and use them correctly.*
6. *Some sentences in the manuscript need to be grammatically corrected.*
   Response: we have looked through again and edited the manuscript as suggested. The manuscript had been reviewed by the proffesional English editing service before the submission and the certificate was submitted with the manuscript.

7. *The information about the ethical approve of the research need to be shown in the article.*
   Response: Further information on the ethical approval has been added in the manuscript. (line 120 – 123).

8. *What is your background reasons to use Et/An ratio instead of T/DHTratio in diagnosing 5ARD2 patients and carriers? It is necessary to mention leading causes of Et/An ratio in the introduction.*
   Response: The study's background has been added and revised in the introduction accordingly. (line 68 – 87)

9. *In tables, there are some information about the marriage of the patients. If it is an influential factor, please mention how it affects the patients and carriers? If it is not an influential factor, the data about marriage is extra data listed in the table.*
   Response: we agree that the variable about marital status was not an influential factor. The variable has been ommitted from the Table 1.

Reviewer 2

- *The main purpose of this article is to evaluate the feasibility of replacing the Et/An ratio instead of T/DHTratio in diagnosing 5ARD2 patients and carriers; However, there is no clear explanation about the role of the Et/An ratio in this deficiency. Also, there is no reason other than cost for this offer. It is better to add supplementary explanations in this regard to the introduction.*
  Response: further explanations on the Et/An ratio role in diagnosing 5ARD2 cases and carriers have been added accordingly. (line 78 – 85).

- *Information needs to show the ethical approve of the research.*
  Response: Further information on the ethical approval has been added in the manuscript. (line 120 – 123).

- *According to the authors' previous research, which is also mentioned in this article (i.e. ref. 18), the article has no innovation aspect and can be presented as a report or short letter. Otherwise, please specify the new aspects of the article.*
  Response: the article (ref. 18) mentioned about the importance of molecular analysis in the diagnosis of SRD5A2 cases as it is needed as confirmatory test. However, in clinical setting the use of molecular test is still considered costly and is not readily available in the whole region, especially in the rural area. Therefore, other test is warranted to be implemented and to fill the gap in diagnosis of 5ARD2 cases, and carriers as well. This issue is explained further in the discussion. (line 238 – 244)

- *Some data seems to be missed on methods and results and we just encountered them in tables or discussion. For example:*

  - Determining the clinical phenotypic effect of the external genitalia with the external genitalia masculinization scores (EMS), which is not mentioned in the text but can be seen in the table.
  Response: The determination of EMS is accordingly added in the method. (line 109 – 113)

- *- In the introduction and methods section, the type of amino acid mutations in steroid 5-alpha-reductase2)SRD5A2(and its role in pathogenicity were not discussed, but in the discussion section, it is mentioned without prior explanation.*
  Response: the study method has been updated with explanation on our simultaneous study, which revealed the molecular variations in the SRD5A2 gene in our cases. (line 96 – 100)

- *There is no explanation in the manuscript about the reason for the importance of marriage mentioned in the table.*
  Response: we agree the marital status was not an influential variable and has ommitted the variable from table 1.

- *Participants and their details are not mentioned in the method.*
  Response: the methods has been revised accordingly. The recruitment of study participants has been mentioned. (line 103 – 109)

- *It is better to briefly mention the technical methods, even though they are according to conventional or reference methods.*
  Response: the methods of hormonal analysis has been updated and explained briefly. (line 138 – 147)

- *In comparison between Tables 1 and 2, there is not significant change in the Et/An ratio between patients and carriers groups (1.19 Vs 1.28). Given the focus on the ratio mentioned as an indicator of disease diagnosis, how do you justify this?*
  Response: the explanation on this issue has been added in the discussion. (line 220 – 226)

- *Reading the manuscript title, it seems that the authors' goal is simply to compare the two ratios in diagnosing the disease. But in the text, the main goal is the feasibility of replacing the two ratio. If this interpretation is correct, it is better to change the title.*

  Response: we agree to change the title as suggested. Thank you

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Mehdi Hedayati: Associate Editor | **Revision** (1) 5 Mar 2021

Dear EIC,
Thanks to the authors of the manuscript, the corrections made and the answers to the questions are accepted.
So, in my opinion, it can be considered for publication.
Thanks.

REFEREE: EIC | **Revision** (1) 10 Mar 2021

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.