OPEN PEER REVIEW

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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
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- 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

Gene, Cell and Tissue
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Peer Review Report for "Sperm DNA Damage and Protamine Transcripts Content in Iranian Men with Unexplained Infertility"

Author(s): Mehran Dorostghoal, Hamid Galehdari, Masoud Hemadi, Saba Abdi

Review Timeline:

Submit Date: 19 Mar 2021
Revised Date: 3 May 2021
Accepted Date: 19 May 2021

Revision (0)

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

REFEREE: Reviewer | **Revision** (0) 5 Apr 2021

Dear AE,
Comments on a manuscript entitled" Sperm DNA damage and protamine transcripts content in Iranian men with unexplained 3 infertility"
1. What is the novelty of this research?
2. Please choose the keyword base on MESH.
3. Please add inclusion and exclusion criteria.
4. The last line of the semen analysis part does not have the reference.
5. The sample size is too little to conclude the result.
6. Please check the arrows in figure 1.
7. Suggestions and limitations should be added
Thanks.

REFEREE: Reviewer | **Revision** (0) 10 Apr 2021

Dear AE,
Comments on a manuscript entitled " Sperm DNA damage and protamine transcripts content in Iranian men with unexplained infertility" for the GCT.
This study evaluated the sperm DNA damage and protamine transcripts content in Iranian

normozoospermic fertile and infertile men. The author analyzed DNA damage using comet assay and transcript levels of PRM1 and PRM2 in ejaculated spermatozoa assessed by quantitative real-time PCR. They showed the prognostic value and clinical utility of the sperm DNA damage and protamine transcripts content for the discrimination between healthy fertile and unexplained infertile men. However, in recent years, several studies have been conducted on Sperm DNA damage, and the present study does not provide new information in this regard. Eventually, it is a repetition of previous studies and lacks novelty. If not, please introduce the highlights of the MS. Also, the MS needs some major revisions as follow:

1. The english language of the manuscript is not sufficient and English editing is highly recommended.
2. All abbreviations should be defined when they are used for the first time, in addition, all abbreviations used in each table should be defined below that table.
3. Keywords should be selected from MeSH Headings, not MeSH entries. You can find the appropriate keywords on "Mesh Browser" at "https://meshb.nlm.nih.gov/search".
4. Use the same pattern to write the article. The author should pay attention to the main format of the journal and references.
5. The number of participants in this project (patients and healthy) is very small. How is this number calculated, Infertile men (n=17), Healthy fertile volunteers (n=10)? Measure the study power.
6. The final conclusion still needs correction. The most important details of the study should be mentioned.
7. Half of the references are old. It is better to use newer references.

Final decision: major revision.

Kindest Regards

Azam Asemi Rad: Associate Editor | **Revision** (0) 13 Apr 2021

Dear EIC,

Thanks for submitting the manuscript entitled" Sperm DNA damage and protamine transcripts content in Iranian men with unexplained infertility". The review process is completed, and all thorough reviews are included. The reviewers found considerable concerns like lack of novelty and some issues in the method part. The manuscript also needs English editing.

yours faithfully,

Zahra Heidari: EIC | **Revision** (0) 17 Apr 2021

Dear Authors,

Based on the reviewers' comments and as I read, this manuscript needs major revisions and reply to the comment point by point. English language editing also must be done.

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.

Editor-in-Chief of Gene, Cell and Tissue

Dear Professor Dr. Heidari

We would like to thank you for the opportunity to revise our manuscript **(113112)** entitled "**Combined first-trimester screening of trisomy 21 in women with different age in Southwest Iran**". We carefully considered the comments offered by dear reviewer. Herein, we explain how we revised the paper based on those comments and recommendations;

Reviewer 1

1. Comment: Present study does not provide new information in this regard. Eventually, it is a repetition of previous studies and lacks novelty. If not, please introduce the high lights of the MS.

Response: Thank you very much for this point.

Numerous tests have been introduced to analyze sperm DNA fragmentation such as Comet, TUNEL SCSA and SCD. While there are benefits to each test and debate about their relative effectiveness, comet assay is the best predictor of male infertility (*). In present study we used comet assay to analyze sperm DNA fragmentation.

Moreover, there is growing evidence that multiple geographical, environmental and lifestyle factors can act alone or in combination could affect men reproductive health (**). This study for the first time investigated sperm DNA integrity and protamine transcript levels in Southwest Iran and presented the degree of SDF and protamine transcripts ratios in unexplained infertile men.

***Javed A, Talkad MS, Ramaiah MK. Evaluation of sperm DNA fragmentation using multiple methods: a comparison of their predictive power for male infertility *Clin Exp Reprod Med*. 2019;46(1):14-21.**

**** Rahban, R., Nef, S. Regional difference in semen quality of young men: a review on the implication of environmental and lifestyle factors during fetal life and adulthood. *Basic Clin. Androl.* 30, 16 (2020).**

**** Palani A, Sengupta P, Agarwal A, Henkel R. Geographical differences in semen characteristics: Comparing semen parameters of infertile men of the United States and Iraq. *Andrologia*. 2020;52(3). doi:10.1111/and.13519.**

2. Comment: The English language of the manuscript is not sufficient and English editing is highly recommended.

Response: Thank you very much for your suggestion. We have made careful modifications to the original manuscript and carefully proof-read the manuscript to minimize typographical and grammatical errors and highlighted the words in the revised manuscript.

3. Comment: All abbreviations should be defined when they are used for the first time, in addition, all abbreviations used in each table, should be defined bellow that table.

Response: Thank you very much for this point. We corrected all abbreviations in the manuscript and tables.

4. Comment: Keywords should be selected from MeSH Headings, not MeSH entries. You can find the appropriate keywords on "Mesh Browser" at "https://meshb.nlm.nih.gov/search".

Response: Thank you very much for your suggestion. We checked and corrected the keywords according to MeSH Headings.

5. Comment: Use the same pattern to write the article. The author should pay attention to the main format of the journal and references.

Response: Thank you very much for this comment. We checked and corrected manuscript according to the format of **Gene, Cell and Tissue** journal.

6. Comment: The number of participants in this project (patients and healthy) is very small. How is this number calculated, Infertile men (n=17), Healthy fertile volunteers (n=10)? Measure the study power.

Response: Thank you very much for this point. Sample size in this study was determined based on previous studies, and it is small because of the low participation of individuals in this experiment (especially fertile couples), ethical considerations and limited time (MSc thesis). We explained the limitation of present study and suggested that this study needs to be investigated in a larger sample size in the "**Discussion**" section.

7. Comment: The final conclusion still needs correction. The most important details of the study should be mentioned.

Response: Thank you very much for this comment. We added some detailed explanations in "**Conclusion**" section.

8. Comment: Half of the references are old. It is better to use newer references.

Response: Thank you very much for suggestion. We tried to compare and discuss our findings with available results, however as much as possible we searched **2** newer references and replaced them.

Reviewer 2

1. Comment: What is the novelty of this research?

Response: Thank you very much for this point.

Numerous tests have been introduced to analyze sperm DNA fragmentation such as Comet, TUNEL SCSA and SCD. While there are benefits to each test and debate about their relative effectiveness, comet assay is the best predictor of male infertility (*). In present study we used comet assay to analyze sperm DNA fragmentation.

Moreover, there is growing evidence that multiple geographical, environmental and lifestyle factors can act alone or in combination could affect men reproductive health (**). This study for the first time investigated sperm DNA integrity and protamine transcript levels in Southwest Iran and presented the degree of SDF and protamine transcripts ratios in unexplained infertile men.

***Javed A, Talkad MS, Ramaiah MK. Evaluation of sperm DNA fragmentation using multiple methods: a comparison of their predictive power for male infertility *Clin Exp Reprod Med*. 2019;46(1):14-21.**

**** Rahban, R., Nef, S. Regional difference in semen quality of young men: a review on the implication of environmental and lifestyle factors during fetal life and adulthood. *Basic Clin. Androl.* 30, 16 (2020).**

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2. Comment: Please choose the keyword base on MESH.

Response: Thank you very much for this point. We corrected all abbreviations in the manuscript and tables.

3. Comment: Please add inclusion and exclusion criteria.

Response: Thank you very much for this suggestion. We added inclusion and exclusion criteria in the "**Methods**" section.

4. Comment: The last line of the semen analysis part does not have the reference.

Response: Thank you very much for your suggestion. We checked and added reference number at the end of this sentences.

5. Comment: The sample size is too little to conclude the result.

Response: Thank you very much for this comment. Sample size in this study was determined based on previous studies, and it is small because of the low participation of individuals in this experiment (especially fertile couples), ethical considerations and limited time (MSc thesis). We explained the limitation of present study and suggested that this study needs to be investigated in a larger sample size in the "**Discussion**" section.

6. Comment: Please check the arrows in figure 1.

Response: Thank you very much for this point. We checked the "**White and Red Arrows**" in Figure 1.

7. Comment: Suggestion and limitation should be added.

Response: Thank you very much for this comment. We added the limitation and suggestion in "**Conclusion**" section.

Best regards,

OPEN PEER REVIEW

Revision (1)

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

REFEREE: Reviewer | **Revision** (1) 15 May 2021

Dear AE,
The authors modified all parts of the manuscript which the reviewers mention and added some new information as well and this version of the manuscript is appropriate for accepting.
Thanks.

Azam Asemi Rad: Associate Editor | **Revision** (1) 15 May 2021

Dear EIC,
Thanks for submitting the article titled "Sperm DNA damage and protamine transcripts content in Iranian men with unexplained infertility " and giving us the opportunity to assess your work. The reviewers were overall satisfied with the revised manuscript. The gene, cell, and tissue journal is pleased to announce this manuscript's acceptance for publication.
Regards,

Zahra Heidari: EIC | **Revision** (1) 19 May 2021

Dear Author,
Based on the reviewer's and AE's comments, revisions were done well. Thus this manuscript can be accepted for publication in GCT.
Thanks.