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Response to Reviewers

Dear Editors-in-chief,

Thank you for giving us the opportunity to submit a revised draft of the manuscript "Leptin Levels in Women with Unexplained Infertility: A Systematic Review and Meta-Analysis" for publication in the World Journal of Meta-Analysis. We appreciate the time and effort that you and the reviewers dedicated to providing feedback on our manuscript and are grateful for the insightful comments on and valuable improvements to our paper.

We have incorporated most of the suggestions made by the reviewers. Those changes are highlighted within the manuscript. Please see below, for a point-by-point response to the reviewers' comments and concerns. All page" **P**" and lines "**L**" numbers in read refer to the revised manuscript file with tracked changes.

Here is a point-by-point response to the reviewers' comments and concerns.

Reviewer #1:

Comment: In this article, the authors included 6 studies that fulfilled the eligibility criteria and conducted a META-analysis, which found that women with unexplained infertility had significantly higher leptin levels than fertile women. This result suggested that leptin might be a potential biomarker for women UI that could help identify women with a high risk of infertility. This article has certain clinical value. To be honest, they did a good".

Response: Thank you very much for these comments, I humbly accept them.

Reviewer #2:

Comment: The objective of the present manuscript, a systematic review and meta-analysis was aimed to find serum leptin levels in women with unexplained infertility and arrived at a conclusion, that the elevated leptin levels were detected in women with UI compared with fertile women, hence, leptin could be a potential biomarker for UI in women, and may be useful for identifying women with a high risk of infertility. It is a well conducted review with a proper use of qualitative assessment and regression analysis**,** however the authors advised to give more focus in explaining the link between adipose tissue and reproductive system and concern regarding serum leptin levels in infertile and fertile women before addressing UI.

Response: We thank you for this useful suggestion. As suggested by the reviewer, we have changed it **P3&4/L76-91.**

Comment: The manuscript elaborated a Meta-Analysis of Leptin levels in women with infertility. An interesting study with an accurate methodology.

Response: Thank!

Comment: The quality of Figure 1 is not enough and needs to be updated.

Response: Totally agree, we have accordingly updated Fig 1 quality.

Comment: What are the inclusion and exclusion criteria of the author? Please add

Response: Honestly, I didn't fully understand this point, but if you mean the inclusion and exclusion criteria of the study, we already added it under (Eligibility criteria and now change it to Inclusion and exclusion criteria (**P4/L101**), but if you mean the inclusion and exclusion criteria of authors in the author's list, we already put a whole section called "Authors' contributions" to identify their roles in this manuscript (**P12/L289-295**), according to ICMJE guidelines.

Comment: Do different methods of measuring leptin really have no effect?

Response: It should have an effect on the leptin value, but the difference between the two groups is still the same. Also, when we check the source of heterogeneity, we didn't find any statistically significant effect of the methods of measuring on the final result.

Comment: Forest plot (random-effects model) or circulating leptin levels and unexplained infertility, the results showed no significant effect?

Response: The possible results of this study are: Leptin is higher in the UI group than it in the control group (Fertile women), or the leptin is lower in the UI group than it in the control group (Fertile women), or the leptin concentration isn't affected by UI. Hence, the result of this study gives us a strong argument that the women with unexplained infertility have a higher serum level of leptin compared with fertile women, but still because the majority of included studies were observational studies this argument still has some weakness and is not one hundred percent definitive, and need t more experimental studies.

Comment: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Meta-Analysis, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments, and the Criteria for Manuscript Revision by Authors. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thank you for the suggestions. We have made the proposed changes in the manuscript.

Additional clarifications

In addition to the above comments, all spelling and grammatical errors pointed out by the reviewers have been corrected. We look forward to hearing from you in due time regarding our submission and to respond to any further questions and comments you may have.

Sincerely, Correspondent author 17/12/2021

1 HOW DO AUTHORS CORRECTLY DEAL WITH THEIR PEER-REVIEW REPORT AND COMMENTS RAISED BY THE SCIENCE EDITOR? YES or NO
1.1 Authors should reconsider the strengths and weaknesses of their manuscript. [YES]
1.2 Authors should carefully read the peer-review report. [YES]
1.3 Authors should carefully answer reviewers. [YES]
1.4 Authors should carefully format their manuscript. [YES]
1.5 Authors should carefully polish the language of their manuscript. [YES]
2 FIRST SECTION OF WRITING REQUIREMENTS YES or NO
2.1 Title [Leptin Levels in Women with Unexplained Infertility: A Systematic Review and Meta-Analysis]

2.2 Running title [Leptin Levels in Women with Unexplained Infertility]

2.3 Authorship [Abdullah A. A, Musa Ahmed, Adesina Oladokun]

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2.6 Author contributions [AA, MA, and AO conceived and designed the review. AA, MA and AO carried out the draft of the manuscript and AA is the guarantor of the review. AA, MA and AO developed the search strings. AA, MA and AO screened and selected studies. AA and MA extracted the data. AA and MA evaluated the quality of the studies. AA and MA carried out analysis and interpretation. AA, MA, and AO rigorously reviewed the manuscript]

2.7 Supportive foundations [No]

2.8 Conflict-of-interest [The authors declared no potential competing of interest concerning the research, authorship, and/or publication of this article]

2.9 PRISMA 2009 Checklist [YES]

2.10 Open-Access [Yes]

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2.12 Abstract [YES]

2.13 Key words [Leptin, Meta-analysis, Serum level, Unexplained infertility, Women]

2.14 Copyright [YES]

2.15 Core tip [YES]

2.16	Audio core tip	[YES]
3 SECOND SECTION OF WRITING REQUIREMENTS		YES or NO
3.1	Main text	[YES]
3.2	Biostatistics	[YES]
3.3	Units	[YES]
3.4	Illustrations	[YES]
3.5	Tables	[YES]
3.6	Notes in illustrations and tables	[YES]
3.7	Abbreviations	[YES]
3.8	Italics	[]

3.9 Article highlights [YES]

3.10	Acknowledgements	[YES]
3.11	References	[YES]

4 ETHICS AND RELEVANT DOCUMENT(S) REQUIRED FOR META-ANALYSIS NO

5 LANGUAGE EDITING FOR MANUSCRIPTS SUBMITTED BY NON-NATIVE SPEAKERS OF ENGLISH YES

6 COPYRIGHT LICENSE AGREEMENT YES

7 CONSEQUENCES OF MODIFICATIONS AFTER THE FORMAL ACCEPTANCE YES