Review of: "Effect of Supplementation with Moringa oleifera on Antioxidant and Oxidative Stress Biomarkers of Infertile Women: A Pilot Open-Label Randomized Clinical Trial"

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Potential competing interests: No potential competing interests to declare.

Dear Author, I have reviewed v1 and am currently looking at v2. Should any suggestions from v1 not have been addressed, I will include the suggestions again here.

For v2, suggestions for improvement:

1. The plant name '*Moringa oleifera'* needs to be standardized throughout the article, with the capital 'M' and entire term italicized. Introduce the abbreviation '*M. oleifera'* in the abstract and introduction sections, and consistently use it throughout the article. There is no need to use the abbreviation 'MO', instead, use 'M. oleifera' consistently.
2. The term 'oxidative stress' can be written as it is without the 'OS' abbreviation.
3. **Introduction:**

   - Suggest to cite the WHO website directly for the definition of infertility "Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse".

   - In the second sentence of paragraph 6, the phrase "Studies on human and animal models…" requires citations from primary human and animal studies instead of relying on a review. The review currently cited in support of this sentence is from 2005, and I recommend replacing it with a more recent study.

   - The discussion on ROS and pathological mechanisms can be condensed into fewer paragraphs. Currently, there are four paragraphs dedicated to this topic.

   - The reference provided for last sentence of paragraph 9 "Plott, E.G (2017). Moringa Helps My Energy While I Go Through Menopause. Available at: http://plottpalmtree.miiduu.com/menopause accessed on 8th August, 2023" does not appear to be from a scientific journal or reputable database. Instead, it seems to be from a personal website or blog. Therefore, it may not meet the standards for academic or scientific citation.

   - In paragraph 10, the discussion on potential effects of*M. oleifera* on hormones and the hypothalamic-pituitary axis could be placed after the ROS paragraph above because it discussed the mechanisms by which the herb can act upon as well. For paragraph 10, I suggest focusing on current research done for *M. oleifera*, particularly human randomized-control trials (RCTs). It's important to describe any ongoing RCTs and summarize existing findings, emphasizing whether there have been studies specifically investigating infertility. If there are no RCTs on infertility, this should be clearly stated.

4. **Methodology:**

   - In Figure 1, the reasons for loss to follow-up should be stated either in the figure or in a paragraph. Were all the patients unable to return for the supplements, or were there any adverse effects causing them to withdraw themselves? With a dropout rate of 33%, which is high, there will be less statistical power, making it difficult to determine whether any differences between groups are truly significant, especially given the small sample size.
   - One more detail of the *M. oleifera* supplements that can be added include whether the capsules were from raw leaf powder or leaf extracts. If leaf extracts, you can name the solvent used for the extract, for example, ethanol or aqueous extract.

5. **Results:**

   - The baseline characteristics of the patients included into the study should be reported. These may include their mean age, body mass index, blood pressure, duration of infertility, exercise status, smoking or alcohol consumption, and any other relevant baseline factors assessed during the study.
   - Reporting on whether any adverse effects were observed throughout the study is necessary.
   - The results suggest that the only significant differences observed were slight variations in certain oxidative stress markers between fertile and infertile women. However, no statistically or clinically significant differences were found in oxidative stress markers between infertile women receiving supplementary *M. oleifera* and those who did not.

6. **Discussion, recommendations, and limitations:**

   - The fifth paragraph of the discussion section describes some limitations of the study such as sample size and dropouts. I suggest combining the ‘limitation of the study’ section into the discussion section and remove the ‘limitations of the study’ section.
   - The discussion explores the potential contribution of *M. oleifera* as an antioxidant. However, this study failed to demonstrate such an effect, as infertile women receiving the supplement showed no significant difference in oxidative stress markers compared to those who did not. Therefore, in my opinion, the recommendation considering a larger-scale population study to replicate or refine these findings (by increasing sample size with hopes of demonstrating a positive effect) may not be necessary unless the underlying issues of poor trial design (open-label, high dropout rate) are addressed and significant improvements in oxidative stress markers are demonstrated.

7. **References:** Some references are incomplete and inconsistent in their formatting, such as variations in listing all authors or using ‘et al’. For example, “Sang Q, Ray PF, Wang L. (2023). Understanding the genetics of human infertility” is incomplete. The formatting for the references like “Koracevic D, Koracevic G, Djordjevic V, et al (2001).” and “Halliwell B., (2001)." is inconsistent. The reference list should be revised to align with the guidelines of the intended journal for publication.