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International Journal of Advanced Research

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REVIEWER'S REPORT

Manuscript No.: IJAR-58502

Title: Tamoxifen Provides Comparable Reproductive Outcomes and Improved Endometrial Development Compared with Clomiphene Citrate: Findings from a Three-Arm Randomized Trial in Women with Polycystic Ovary Syndrome,

Recommendation:
Accept as it is .....
Accept after minor revision.....
Accept after major revision...YES.....
Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality		_		
Techn. Quality			_	
Clarity		_		
Significance		_		

Reviewer's ID: JPR-

Detailed Reviewer's Report

Reviewer's Report

Overall Assessment

The manuscript presents a prospective randomized comparative study evaluating clomiphene citrate, tamoxifen, and gonadotropins for ovulation induction in women with PCOS. The topic is clinically relevant, particularly for resource-limited settings where letrozole may not be readily available. The manuscript is generally well organized and written; however, several methodological and reporting issues require revision before publication.

Strengths

*1. **Clinically relevant topic** addressing ovulation induction in women with PCOS.*

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*2. **Prospective randomized three-arm design**, improving internal validity.*

*3. Inclusion of **three commonly used treatment modalities** allows meaningful comparison.*

*4. **Current literature** and the 2023 International PCOS Guideline are appropriately cited.*

*5. Both **efficacy and safety outcomes** are evaluated.*

6. Endometrial thickness is included as a clinically meaningful secondary outcome.

7. Discussion appropriately relates findings to previous studies.

8. Conclusions are generally supported by the reported results.

Weaknesses

*1. **Small sample size (n = 90)** limits statistical power.*

*2. **Single-center study**, reducing generalizability.*

3. Randomization method is insufficiently described (allocation concealment not reported).

*4. No information regarding **blinding** of investigators or outcome assessors.*

*5. No **sample size or power calculation** provided.*

6. Live birth rate, the most important reproductive outcome, was not assessed.

7. The study period (2016–2017) is relatively old, although the discussion is updated with current guidelines.

8. Statistical reporting is incomplete:

  ** Confidence intervals are absent.*

  ** Effect sizes are not reported.*

9. Table 3 contains an obvious error:

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" "Mild OHSS = XX" instead of numerical data.

10. Adverse events require more detailed reporting.

11. Trial registration number is not provided.

12. No CONSORT flow diagram is included.

13. Figures illustrating participant flow or outcome comparisons would strengthen the manuscript.

Key Points

**** Tamoxifen achieved **ovulation and pregnancy rates comparable** to clomiphene citrate and gonadotropins.***
**** Tamoxifen demonstrated **significantly greater endometrial thickness**, suggesting improved endometrial receptivity.***
**** No significant differences were observed in pregnancy outcomes among treatment groups.***
**** Safety profile was generally favorable with no severe OHSS.***
**** Tamoxifen may serve as an effective alternative oral ovulation induction agent when letrozole is unavailable.***

Significance

The study contributes useful clinical evidence regarding the role of tamoxifen in ovulation induction among women with PCOS. Given the increasing preference for

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letrozole, contemporary comparative data on tamoxifen remain limited. The findings are particularly valuable for clinicians practicing in low- and middle-income countries where treatment availability and affordability influence therapeutic choices.

However, the study's impact is limited by the modest sample size, single-center design, and incomplete methodological reporting.

Major Comments

1. Describe the randomization process in greater detail, including allocation concealment.
2. State whether investigators or ultrasonographers were blinded.
3. Include a sample size calculation.
4. Add a CONSORT flow diagram.
5. Correct Table 3 (replace "XX" with actual data).
6. Report confidence intervals and effect sizes alongside p-values.
7. Provide additional details on adverse events.
8. Clarify whether analyses were intention-to-treat or per-protocol.
9. Explain why live birth outcomes were unavailable.
10. Discuss potential selection bias and study limitations in greater depth.

Minor Comments

1. Correct formatting inconsistencies throughout the manuscript.

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2. Ensure uniform spacing around citations.

3. Standardize table formatting.

4. Improve grammar in a few sentences.

5. Define abbreviations at first appearance.

6. Carefully proofread the manuscript before submission.

Recommendation

*****Major Revision*****

Justification

Although the study addresses an important clinical question and has a sound prospective randomized design, several methodological and reporting deficiencies must be corrected before publication. These include incomplete reporting of randomization, absence of a sample size calculation and CONSORT diagram, incomplete statistical reporting, an error in the safety outcomes table, and insufficient reporting of adverse events. Addressing these issues will substantially improve the scientific quality, transparency, and reproducibility of the manuscript.

Below is a **line-by-line reviewer justification** explaining why the manuscript warrants **Major Revision** rather than minor revision. The comments are based on the manuscript you uploaded.

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Line(s)	Issue Identified	Why it Requires Major Revision
64–68	Ethics approval mentioned, but **approval number** is missing.	Most journals require the Institutional Ethics Committee approval/reference number for transparency and ethical compliance.
64–91	Randomization described only as "computer-generated"; **allocation concealment** is not explained.	Without allocation concealment, selection bias cannot be excluded. This is a major methodological deficiency in an RCT.
64–132	**Blinding** of participants, clinicians, or outcome assessors is not reported.	Lack of information on blinding raises concerns regarding performance and detection bias.
69–132	**Sample size calculation** or power analysis is absent.	Reviewers cannot determine whether 90 participants provide sufficient statistical power to detect meaningful differences.
69–132	**Clinical trial registration number** is missing.	Registration is expected for randomized clinical trials in many journals and improves transparency.
124–131	Statistical methods include ANOVA and Chi-square tests, but **confidence intervals and effect sizes** are not reported.	Modern reporting standards require effect estimates with confidence intervals, not only p-values.
135–138	The manuscript states all patients completed the study, but **no CONSORT flow diagram** is provided.	CONSORT flowcharts are standard for randomized trials and improve reporting quality.
139–146	Baseline characteristics include only age, BMI, and infertility duration.	Important baseline reproductive and hormonal variables (e.g., AMH, LH, FSH, testosterone, PCOS phenotype) are missing, limiting comparability.
147–164	Only percentages are presented for treatment outcomes.	Absolute numbers, confidence intervals, and adjusted analyses should be provided for better interpretation.
165–166	**Table 3 contains "XX"** for Mild OHSS.	This is an obvious error indicating incomplete data reporting and must be corrected before publication.
167–172	Safety outcomes are insufficiently detailed.	The manuscript does not adequately describe adverse events, withdrawals due to toxicity, or severity grading.
173–176	Authors conclude comparable efficacy although differences are	Non-significant findings should be interpreted cautiously unless equivalence

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	statistically non-significant.	or non-inferiority was specifically designed and powered.
180–241	Discussion does not adequately address important methodological limitations.	The implications of single-center design, lack of blinding, and limited sample size should be discussed in greater depth.
243–252	Authors acknowledge some limitations but omit several others.	Missing discussion of allocation concealment, absence of trial registration, and missing effect-size reporting weakens transparency.
247–252	**Live birth**, the most clinically relevant fertility outcome, was not evaluated.	Clinical pregnancy alone is an intermediate outcome; live birth is preferred in reproductive medicine.
Entire manuscript	No supplementary material, protocol, or statistical analysis plan is referenced.	Reproducibility is limited without access to detailed protocol information.
Entire manuscript	Several formatting issues (spacing, punctuation, table formatting, citation consistency).	These require editorial correction before publication.

Why** Major Revision **instead of Minor Revision?

The manuscript should be classified as **Major Revision** because several issues affect the **scientific rigor and reporting quality**, not just language or formatting:

Incomplete reporting of the randomized trial methodology.

No sample size/power calculation.

Missing allocation concealment and blinding details.

Missing CONSORT flow diagram.

Incomplete statistical reporting (no confidence intervals/effect sizes).

Error in the safety outcomes table ("XX").

Lack of trial registration information.

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Important clinical outcome (live birth) not assessed.

Safety reporting requires expansion.

Discussion of study limitations needs strengthening.

These issues require substantial revision of the manuscript rather than simple editorial corrections, while the study design and results remain potentially suitable for publication after appropriate revision.