Systematic Review

Article Category: Systematic Review and Meta-Analysis Effectiveness Comparison of Letrozole versus Metformin for Ovulation Induction in Women with PCOS

I Komang Tri Yasa Widnyana,[1] Aditya Prabawa,[2] Putu Ayu Sintya Dewi[3]
[1]Faculty of Medicine, Ganesha Education University, Bali, Indonesia
[2]Department of Obstetrics and Gynecology, Faculty of Medicine, Ganesha Education University, Bali, Indonesia
[3]Faculty of Medicine, Brawijaya University, Malang, Indonesia
Correspondence: I Komang Tri Yasa Widnyana, tri.yasa@student.undiksha.ac.id
Received: March 15, 2026 | Accepted: July 2, 2026 | Published: July 10, 2026

Abstract
Objective: This study serves to compare the effectiveness of letrozole and metformin for ovulation induction in women with polycystic ovary syndrome based on ovulation, pregnancy, and live birth outcomes.
Methods: This study was conducted as a systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Literature searches were performed in PubMed, Scopus, Web of Science, the Cochrane Library, and ScienceDirect. Randomized controlled trials comparing letrozole and metformin in women with polycystic ovary syndrome were included. Primary outcomes included ovulation rate, clinical pregnancy rate, and live birth rate.
Result: Fourteen randomized controlled trials involving 3,314 patients were analyzed. Meta-analysis showed that letrozole significantly improved ovulation rate compared to metformin (odds ratio 1.29; 95% confidence interval 1.09-1.53). Letrozole also demonstrated superior clinical pregnancy outcomes (odds ratio 1.65; 95% confidence interval 1.41-1.93) and higher live birth rates (odds ratio 1.49; 95% confidence interval 1.26-1.75). Metformin primarily improved metabolic parameters but showed limited effectiveness as monotherapy for reproductive outcomes.
Discussion: Letrozole acts directly on ovarian follicular development, whereas metformin mainly improves insulin resistance. These differences explain the superior reproductive outcomes observed for letrozole.
Conclusion: Letrozole is more effective than metformin for ovulation induction and reproductive outcomes in women with polycystic ovary syndrome and should be considered a first-line therapy.

Keywords: Polycystic ovary syndrome; letrozole, metformin; ovulation induction; infertility

Perbandingan Efektivitas Letrozole versus Metformin untuk Induksi Ovulasi pada Wanita dengan PCOS

Abstrak
Tujuan: Penelitian ini bertujuan untuk membandingkan efektivitas letrozol dan metformin dalam induksi ovulasi pada wanita dengan sindrom ovarium polikistik berdasarkan luaran ovulasi, kehamilan, dan kelahiran hidup.
Metode: Penelitian ini merupakan tinjauan sistematis dan meta-analisis yang mengikuti pedoman Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Pencarian literatur dilakukan pada basis data PubMed, Scopus, Web of Science, Cochrane Library, dan ScienceDirect. Uji klinis teracak yang membandingkan letrozol dan metformin pada pasien sindrom ovarium polikistik dimasukkan dalam analisis. Luaran utama meliputi angka ovulasi, angka kehamilan klinis, dan angka kelahiran hidup.
Hasil: Sebanyak 14 uji klinis teracak dengan total 3.314 pasien dianalisis. Meta-analisis menunjukkan bahwa letrozol secara signifikan meningkatkan angka ovulasi dibandingkan metformin (rasio odds 1,29; interval kepercayaan 95% 1,09 - 1,53). Letrozol juga menunjukkan angka kehamilan klinis yang lebih tinggi (rasio odds 1,65; interval kepercayaan 95% 1,41 - 1,93) serta peningkatan angka kelahiran hidup (rasio odds 1,49; interval kepercayaan 95% 1,26 - 1,75). Metformin terutama memperbaiki parameter metabolik hanya saja memiliki efektivitas yang lebih terbatas terhadap luaran reproduksi jika digunakan sebagai monoterapi.
Diskusi: Letrozol bekerja langsung pada perkembangan folikel ovarium, sedangkan metformin terutama memperbaiki resistensi insulin. Perbedaan mekanisme ini menjelaskan keunggulan luaran reproduksi pada terapi letrozol.
Kesimpulan: Letrozol lebih efektif dibandingkan metformin dalam induksi ovulasi dan luaran reproduksi pada wanita dengan sindrom ovarium polikistik.

Kata kunci: Induksi ovulasi; infertilitas; letrozole; metformin; dan sindrom ovarium polikistik,

 DOI:10.24198/obgynia.v9i2.1121

Introduction

Polycystic ovary syndrome (PCOS) is a common gynecological endocrine disorder in women of gestational age, as well as the most common cause of female infertility. PCOS is characterized by symptoms of oligomenorrhea, disorders, amenorrhea, ovulatory dysfunction, infertility, and hyperandrogenism, as well as polycystic ovarian morphology. The syndrome affects women of reproductive age; its global prevalence is estimated at 6-20% depending on the applied diagnostic criteria.[1] The symptoms of the syndrome become contributing factors to anovulatory infertility. Beyond reproductive effects, PCOS-related infertility has significant psychological, social, and economic impacts, which make it a major clinical and public health concern. Ovulation induction represents a cornerstone in the management of infertility in women with PCOS.[2] For decades, pharmacological approaches have targeted modulation of the hypothalamic-pituitary-ovarian axis and improvement of insulin resistance for treatment of PCOS. Metformin, an insulin-sensitizing agent, has long been used to improve insulin resistance, reduce hyperinsulinemia, and restore ovulatory function indirectly.[3] However, metformin monotherapy shows inconsistent effectiveness in improving ovulation and pregnancy, with significant inter-individual variability in response.

Advancements in the understanding of PCOS endocrine mechanisms have identified letrozole, an aromatase inhibitor, as a promising alternative for ovulation induction.[4] Letrozole inhibits androgen-to-estrogen conversion, which reduces negative feedback on the hypothalamus-pituitary axis and increases FSH to stimulate follicular development. However, evidence comparing its effectiveness with metformin remains heterogeneous. Some studies have demonstrated the superiority of letrozole in achieving ovulation and clinical pregnancy, whereas others suggested benefits of metformin in specific subpopulations, such as women with obesity or marked insulin resistance.[5] It becomes necessary to conduct a systematic review and meta-analysis to compare comprehensively the effectiveness of letrozole and metformin for ovulation induction in PCOS, particularly regarding pregnancy outcomes.

Method

1. **Study Design and Registration** ProtocolThis study is a systematic review and meta-analysis conducted according to PRISMA guidelines, with the aim of comparing the effectiveness of letrozole and metformin for ovulation induction in women with PCOS based on ovulation and pregnancy outcomes. The protocol was registered in PROSPERO and is currently awaiting approval.

2. **Search Strategy**
A systematic literature search was conducted across the major databases of PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library, and ScienceDirect from inception to the final search date to identify studies comparing letrozole and metformin for ovulation induction in women with PCOS
.

3. **Study Eligibility Criteria**
. The included studies met predefined eligibility criteria. The population comprised women with PCOS in reproductive age, who were diagnosed using recognized criteria (Rotterdam, NIH, or AES). The intervention was letrozole for ovulation induction (as first-line or after prior treatment failure), with dosing per study protocol. The comparator was metformin, being used as monotherapy or standard

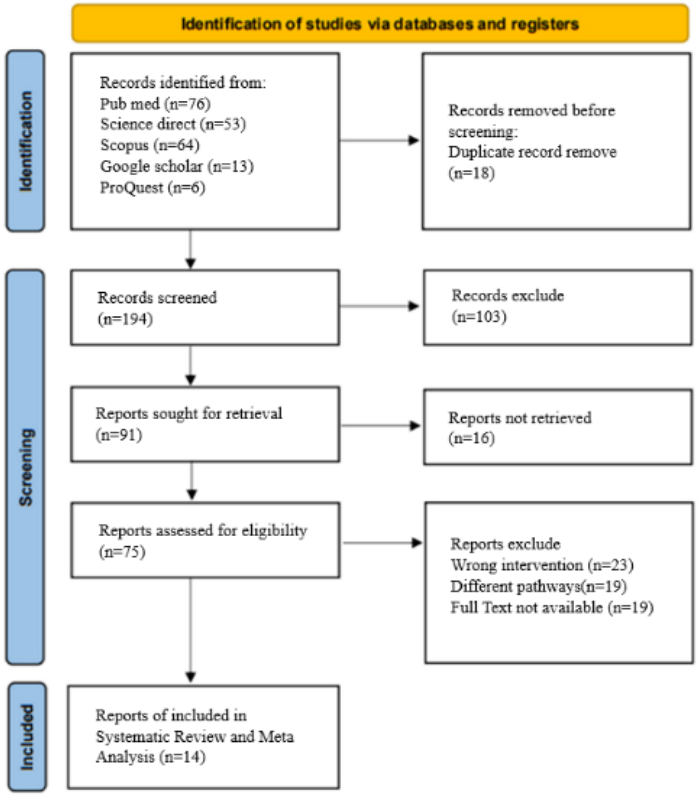

Figure 1 Identification of Studies for the Research

treatment without combination with other ovulation-inducing agents.

4. **Screening and Data Selection Results**
Search results were managed using Rayyan AI for screening and selection. Duplicates were removed through automated detection and manual checking (>90% similarity). The "blind-on" mode was applied to reduce bias. Studies not meeting eligibility based on the title or abstract, lack of full text, or conference abstracts were excluded. The PRISMA flow diagram outlined the selection process and reasons for exclusion. Screening was conducted independently by two reviewers (PASD and AP), with disagreements resolved by a third reviewer (IKTYW).

5. **Data Extraction**
Qualitative and quantitative data were extracted into structured tables using Microsoft Excel 2021 and Rayyan.ai before being reviewed by all authors (IKTYW, PASD, AP). The extracted data comprised study characteristics, design, sample size, participant details (age, BMI, diagnostic criteria), intervention protocols (letrozole and metformin dosage/duration), and clinical outcomes. Primary outcomes involved ovulation and clinical pregnancy rates, while secondary outcomes involved live birth rate, miscarriage rate, and adverse events.

6. **Assessment of Bias and Study Quality**
The methodological quality of included studies was assessed using the QUADAS-2 tool across four risk-of-bias domains and three applicability domains. Three authors independently conducted the assessment, and disagreements were resolved by consensus. Results were recorded in an

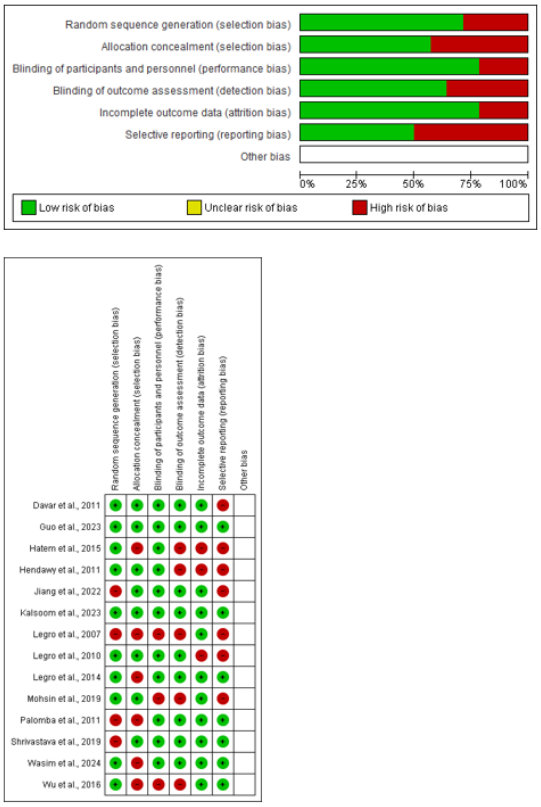

Figure 2 Assessment of Bias and Study Quality

.xlsx file and visualized using ROBVIS for clearer interpretation. Each study was classified as low, unclear, or high risk, as shown in Figure 2.

7. Quantitative Data Analysis

Quantitative data from studies that met the inclusion criteria were synthesized meta-analytically when sufficient clinical and methodological homogeneity across studies were found. The analyzed primary outcomes were ovulation rate, clinical pregnancy rate, and live birth rate. Secondary outcomes comprised miscarriage rate, multiple pregnancy rate, endometrial thickness, time to ovulation, and treatment-related adverse events. For dichotomous outcomes such as ovulation, clinical pregnancy, live birth, miscarriage, and multiple pregnancy, effect sizes were calculated using risk ratios (RRs) with corresponding 95% confidence intervals (CIs). The RR metric was prioritized due to its intuitive interpretation and widespread use in clinical intervention studies. For continuous outcomes, including endometrial thickness and time to ovulation, mean differences (MDs) with 95% CIs were applied when measurement scales across studies were found to be consistent. When different instruments or units were used, standardized mean differences (SMDs) were employed.

Results

1. Search Results and Study Characteristics

Based on 14 primary clinical studies analyzed in this systematic review, letrozole and metformin appeared to play distinct yet complementary roles in ovulation induction strategies for patients with polycystic ovary syndrome (PCOS). Overall, letrozole functioned as the principal ovulation-inducing agent,

Table 1 Study Characteristics

Aspect	Letrozole	Metformin	Combination
Role	First-line ovulation inducer	Adjuvant (metabolic)	Dual approach
Mechanism	↑ FSH → follicle maturation	↑ insulin sensitivity	Combined effects
Ovulation & Pregnancy	Higher, consistent	Lower, variable	Sometimes improved
Best Use	General PCOS	Insulin resistance	Selected subgroups
Key Point	Most effective for reproduction	Limited alone	Not consistently superior

whereas metformin primarily served as an adjuvant therapy that modifies the underlying metabolic and endocrine milieu contributing to PCOS. The study characteristics are presented in Table 1.

Letrozole, which is an aromatase inhibitor, reduces the peripheral conversion of androgens to estrogens; in this way, it attenuates estrogen-mediated negative feedback on the hypothalamic-pituitary axis. This mechanism enhances endogenous follicle-stimulating hormone (FSH) secretion and facilitates dominant follicle maturation. Findings from most comparative studies indicated that letrozole consistently achieves ovulation and clinical pregnancy rates that are at least comparable (or even superior according to several reports) to those with alternative therapies.[6] These effects are attributed to the minimal peripheral anti-estrogenic impact of letrozole, particularly on the endometrium and cervical mucus, which often limit the effectiveness of selective estrogen receptor modulators. Consequently, letrozole has been positioned as a cornerstone therapy for ovulation induction in PCOS across various clinical protocols. In contrast, metformin does not act as a direct ovulation inducer; instead, it targets the pathophysiology of PCOS by improving insulin sensitivity and reducing hyperinsulinemia.[7] Insulin resistance is known to promote ovarian androgen production and disrupt normal folliculogenesis. By lowering levels of circulating insulin and androgen, metformin may improve the ovarian environment and enhance responsiveness to ovulation-inducing agents. However, across the studies that were included in this review, the effect of metformin as monotherapy for reproductive outcomes appeared more limited and inconsistent, particularly when compared with agents that act directly on the reproductive axis.

The combination of metformin and letrozole was evaluated in several studies that are included in the data extraction table, particularly among PCOS populations with more complex metabolic profiles, such as being overweight or obese, having clomiphene-resistant PCOS, or having suspected insulin resistance. Conceptually, this combination targets two key mechanisms simultaneously: stimulation of follicular maturation via letrozole-induced endogenous FSH secretion and optimization of the metabolic-endocrine milieu via metformin. Several studies had reported that the combination improved cumulative ovulation and/or clinical pregnancy rates compared to letrozole on its own.[8] Nevertheless, these benefits were not consistently observed across all trials, and the magnitude of effect varied among studies.

From a clinical perspective, the synthesis of these 14 studies supports an individualized therapeutic approach. Letrozole may be considered the first-line therapy for ovulation induction in most

women with PCOS, whereas the addition of metformin appears more rational in subgroups with overt metabolic disturbances or in patients demonstrating suboptimal response to letrozole monotherapy. This approach aligns with the concept of PCOS as a heterogeneous syndrome, for which treatment response is strongly influenced by clinical and metabolic phenotype.[9]

Although the available evidence provides a comprehensive overview of the respective roles of letrozole and metformin, interpretation of this systematic review should acknowledge several limitations. Differences in outcome definitions (such as ovulation per cycle versus per patient and biochemical versus clinical pregnancy), variability in reporting ultimate outcomes (such as the live birth), and heterogeneous follow-up durations contribute to the heterogeneity among studies.[10] Therefore, these findings underscore the need for further well-designed trials with standardized protocols, consistent outcome reporting, and metabolic phenotype stratification to be able to make a more precise clarification of the role of metformin as an adjuvant to letrozole for ovulation induction in women with PCOS.

2. Meta-Analysis of Ovulation Induction

The forest plot demonstrates that overall, letrozole is more effective than metformin in inducing ovulation among patients with PCOS. Based on the pooled analysis of 14 studies involving 3,314 patients in total (1,679 in the metformin group and 1,635 in the letrozole group), the combined effect estimate showed a pooled odds ratio (OR) of 1.29 (95% CI 1.09-1.53; p = 0.003), which indicates a statistically significant difference in favor of letrozole. This finding suggests that patients treated with letrozole have approximately a 29% higher likelihood of achieving ovulation compared to those receiving metformin. Although several individual studies reported neutral or insignificant results, the majority of effect estimates were consistently oriented toward letrozole being beneficial. Heterogeneity analysis revealed an I^2 value of 61%, which indicates moderate to substantial heterogeneity; this may be attributable to differences in patient characteristics (such as obesity status and insulin resistance), study design, and variations in treatment protocols. Overall, these findings reinforce the role of letrozole as a more effective agent of ovulation induction than metformin, while metformin appears to play a more limited role, primarily as an adjuvant therapy and particularly in subgroups of PCOS patients with prominent metabolic disturbances.

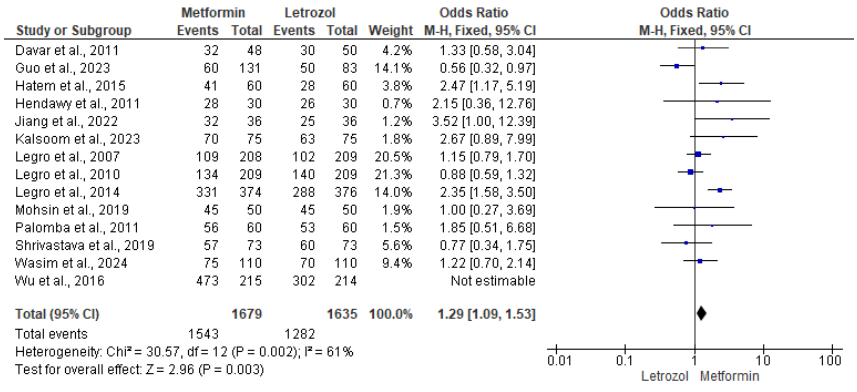

Figure 3 Meta-Analysis of Ovulation Induction

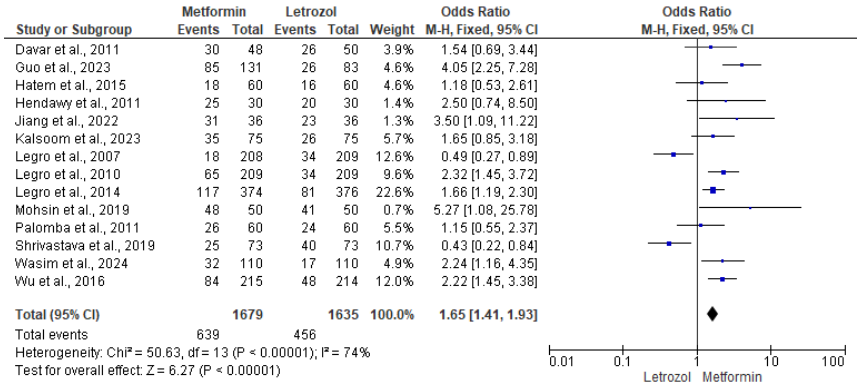

Figure 4 Meta-Analysis of Clinical Pregnancy

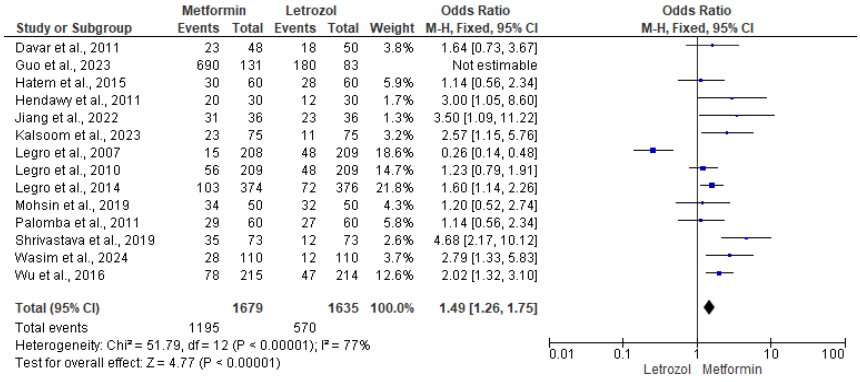

Figure 5 Meta-Analysis of Live Birth

3. **Meta-Analysis of Clinical Pregnancy**
The forest plot indicates that letrozole is significantly more effective than metformin in improving clinical pregnancy rates among patients with PCOS. Based on a meta-analysis of 14 studies that involved 3,314 patients in total (1,679 in the metformin group and 1,635 in the letrozole group), the pooled analysis yielded a combined odds ratio (OR) of 1.65 (95% CI 1.41-1.93; $p < 0.00001$) and demonstrated a strong and statistically significant advantage in favor of letrozole. This finding suggests that PCOS patients treated with letrozole have approximately a 65% higher likelihood of achieving clinical pregnancy, compared to those receiving metformin. Although several individual studies reported neutral effects or results favoring metformin, the majority of effect estimates were consistently oriented toward letrozole being beneficial. The relatively high level of heterogeneity ($I^2 = 74\%$) indicates substantial variability among studies, which may be attributable to differences in patient characteristics (such as obesity status, insulin resistance, or clomiphene resistance), study design, intervention protocols, and follow-up durations. Overall, these findings strengthen the evidence that supports letrozole usage as a superior agent to metformin for achieving clinical pregnancy in ovulation induction among PCOS patients; meanwhile, metformin appears more appropriately positioned as an adjuvant therapy in selected subgroups with prominent metabolic disturbances.

4. **Meta-Analysis of Live Birth**
   The forest plot demonstrates that letrozole is significantly superior to metformin in improving live birth rates among patients with PCOS undergoing ovulation induction.
   Based on a meta-analysis of 14 studies that involved 3,314 patients in total (1,679 in the metformin group and 1,635 in the letrozole group), the pooled effect estimate yielded a combined odds ratio (OR) of 1.49 (95% CI 1.26-1.75; $p < 0.00001$). This indicates that patients treated with letrozole have an approximately 49% higher likelihood of achieving a live birth, compared to those receiving metformin. The majority of individual study effect estimates were oriented in favor of letrozole, although several studies reported neutral findings or could not be included in the pooled estimate due to limited data. The high level of observed heterogeneity ($I^2 = 77\%$) suggests substantial variability among studies, which likely reflects differences in PCOS population characteristics (such as obesity status, insulin resistance, or clomiphene resistance), variations in treatment protocols, and differences in follow-up durations and outcome reporting. Overall, these findings reinforce the evidence that letrozole not only confers advantages in achieving ovulation and clinical pregnancy but also provides a significant benefit in the most clinically relevant endpoint, being live birth. Meanwhile, metformin appears to have a more limited role, which makes it have a better position as an adjuvant therapy in selected subgroups of PCOS patients.

Discussion

1. **Pathophysiology of Polycystic Ovary Syndrome (PCOS)**

Polycystic ovary syndrome (PCOS) is a complex and heterogeneous endocrine-metabolic disorder that is characterized by ovulatory dysfunction, hyperandrogenism, and impaired ovarian folliculogenesis.[11] The pathophysiology of PCOS involves dysregulation of the hypothalamic-pituitary-ovarian axis, which is manifested by relatively increased luteinizing hormone (LH) secretion to follicle-stimulating hormone (FSH) secretion, which promotes excessive ovarian androgen production and inhibits dominant follicle maturation. This condition is further exacerbated by the conditions of insulin resistance and compensatory hyperinsulinemia, which directly enhance ovarian androgen synthesis and reduce hepatic production of sex hormone-binding globulin, which then creates a hyperandrogenic milieu that further disrupts ovulation.[12]

Current management strategies for PCOS are largely symptomatic in their approaches and focus on specific clinical goals, in particular ovulation induction in infertile patients. Letrozole as an aromatase inhibitor reduces circulating estrogen levels and attenuates negative feedback on the hypothalamic-pituitary axis, which leads to increased endogenous FSH secretion and facilitation of dominant follicle development.[13] This mechanism underpins its role as a first-line agent for ovulation induction in PCOS. In contrast, metformin primarily targets insulin resistance and hyperinsulinemia, which has the potential to improve the ovarian endocrine environment and to enhance responsiveness to ovulation induction, although its effects on reproductive outcomes are relatively limited when used as monotherapy.

Combination strategies such as metformin with letrozole are directed for simultaneously addressing the two central

components of PCOS pathophysiology, as ovulatory dysfunction and metabolic disturbance.[14] This approach is theoretically more appropriate for obese or insulin-resistant patients; however, the additional benefit of combination therapy has not been consistently observed across all PCOS populations, which reflects the inherent heterogeneity of the syndrome.[15]

2. Therapeutic Comparison of Letrozole and Metformin in Patients with Polycystic Ovary Syndrome

In the management of infertility due to anovulation in patients with polycystic ovary syndrome (PCOS), metformin and letrozole are a part of two therapeutic approaches that target distinct aspects of the underlying pathophysiology. Letrozole acts directly on the hypothalamic-pituitary-ovarian axis through aromatase inhibition, which leads to reduced circulating estrogen levels and attenuation of negative feedback on the hypothalamus and pituitary gland. This mechanism enhances endogenous follicle-stimulating hormone (FSH) secretion and facilitates dominant follicle maturation; in this way, it functions as a direct ovulation-inducing agent. In contrast, metformin primarily modulates the metabolic component of PCOS by improving insulin sensitivity and reducing hyperinsulinemia, which indirectly decreases ovarian androgen production and improves the endocrine milieu that is supportive of ovulation.

Clinically, the available evidence indicates that letrozole yields superior reproductive outcomes compared to metformin when used as monotherapy for ovulation induction. Letrozole has been consistently associated with higher rates of ovulation, clinical pregnancy, and live birth; this shows its effectiveness in addressing the core folliculogenic dysfunction that underlies anovulatory PCOS. Conversely, metformin as monotherapy demonstrates benefits on reproductive outcomes that are more limited, particularly in patients without prominent metabolic disturbances. However, it remains important for improving metabolic parameters and reducing long-term risks associated with insulin resistance.

These differences in mechanisms of action are also reflected in the safety and tolerability profiles of the two agents. Letrozole is generally well tolerated with its relatively mild and transient adverse effects, whereas metformin is frequently associated with gastrointestinal side effects that may have a negative effect on treatment adherence. Accordingly, in clinical practice, letrozole is more appropriately positioned as a first-line ovulation induction therapy for patients with PCOS, while metformin is more rationally utilized as an adjuvant therapy, particularly for subgroups of patients with obesity or insulin resistance. This approach underscores the importance of personalized treatment selection based on individual clinical and metabolic profiles to optimize reproductive outcomes in PCOS.

3. Clinical Outcome Analysis of Letrozole versus Metformin in Patients with Polycystic Ovary Syndrome

The ovulation rate represents the primary outcome that reflects the immediate success of ovulation induction therapy. Through aromatase inhibition and enhancement of endogenous follicle-stimulating hormone (FSH) secretion, letrozole has consistently demonstrated higher ovulation rates compared to metformin. This finding underscores the direct action of letrozole on the disrupted folliculogenesis characteristic of PCOS. In contrast, metformin improves

ovulation only indirectly by ameliorating insulin resistance and reducing hyperandrogenism; consequently, when used as monotherapy, its effect on ovulation tends to be more limited and highly dependent on a patient's metabolic profile.

The clinical pregnancy rate reflects the subsequent success following ovulation. The majority of available evidence has indicated that letrozole is associated with higher clinical pregnancy rates than metformin. This advantage is likely attributable to the improved ovulatory quality and the minimal peripheral anti-estrogenic effects of letrozole on the endometrium. Although metformin may improve the hormonal milieu, it does not consistently enhance clinical pregnancy rates when used on its own, and its role appears more prominent as an adjunctive therapy. The live birth rate is the most clinically relevant reproductive outcome. Available data have indicated that letrozole not only increases the ovulation and clinical pregnancy rates but also becomes associated with higher live birth rates compared to metformin. This finding suggests that the beneficial effects of letrozole extend to the final pregnancy outcome, whereas the impact of metformin on the live birth rate appears limited without being in combination with other ovulation-inducing agents. Time to ovulation reflects the speed of therapeutic response. Letrozole is generally associated with a shorter and more predictable time to ovulation, which is consistent with its direct mechanism of increasing endogenous FSH secretion. In contrast, metformin requires a longer duration to exert its effects, as its benefits depend on gradual metabolic and hormonal improvements. The miscarriage rate is an important outcome for assessing pregnancy quality. Overall, no consistent or statistically significant difference was observed between letrozole and metformin with respect to miscarriage rates, although some studies suggested a trend toward lower miscarriage rates with therapies that promote a more physiologic endometrial environment. However, definitive conclusions are restricted by the heterogeneity in reporting and limited sample sizes. Adverse effects highlight clear differences in the tolerability of the two treatments. Metformin is frequently associated with gastrointestinal side effects, including nausea, diarrhea, and abdominal discomfort, which could have an adverse effect on patient adherence. Meanwhile, letrozole is generally better tolerated, with side effects such as hot flushes, headache, or fatigue being minor and brief.

Endometrial thickness is an important determinant of implantation success. Letrozole tends to preserve or increase endometrial thickness because it does not exert direct anti-estrogenic effects on endometrial estrogen receptors, in contrast to certain other ovulation-inducing agents. Metformin may exert indirect effects on the endometrium through improvement of the hormonal milieu; however, its impact on endometrial thickness is generally less consistent and less pronounced than the observed impact with letrozole.

4. Relationship Between Clinical Parameters and Reproductive Outcomes

Patient characteristics (age, BMI, and metabolic profile) influence treatment response. Higher BMI and insulin resistance are associated with poorer ovulation and pregnancy outcomes, particularly with metformin monotherapy, while patients with better metabolic profiles respond more favorably to letrozole. Endometrial thickness is a

key factor for implantation. A greater thickness, which is more commonly seen with letrozole, is associated with higher clinical pregnancy and live birth rates as well as possibly lower miscarriage risk. FSH levels directly affect follicular development. Increased FSH enhances follicle maturation and improves ovulation and pregnancy rates, although excessive stimulation may increase the risk of multiple pregnancy. Follicle count and oocyte count reflect ovarian response. Higher counts are associated with improved ovulation and pregnancy outcomes, but excessive follicular response may increase complication risks. Oocyte quality, which is influenced by metabolic status, also plays a role in miscarriage and live birth outcomes. Overall, primary outcomes (ovulation and pregnancy) are mainly driven by FSH levels and follicular response, while secondary outcomes (live birth, miscarriage, complications) are more closely related to endometrial receptivity and metabolic factors.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgments

We would like to express our sincere appreciation to the authors for conducting and presenting this valuable study. The research provides important insights and contributes meaningfully to the advancement of knowledge in this field. The methodology, data analysis, and discussion as presented in the article offer useful perspectives for both clinical practice and future research.

References

1. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JSE, Legro RS, et al. Polycystic ovary syndrome. *Nat Rev Dis Primers*. 2016;2:16057.
2. Balen AH, Morley LC, Misso M, Franks S, Legro RS, Wijeyaratne CN, et al. The management of anovulatory infertility in women with polycystic ovary syndrome. *Endocr Rev*. 2016;37(5):487–525.
3. Palomba S, Falbo A, Zullo F, Orio F. Evidence-based and potential benefits of metformin in the polycystic ovary syndrome: a comprehensive review. *Endocr Rev*. 2009;30(1):1–50.
4. Casper RF, Mitwally MFM. Aromatase inhibitors for ovulation induction. *J Clin Endocrinol Metab*. 2006;91(3):760–71.
5. Franik S, Eltrop SM, Kremer JAM, Kiesel L, Farquhar C. Aromatase inhibitors for subfertile women with polycystic ovary syndrome. *Cochrane Database Syst Rev*. 2018;5:CD010287.
6. Amer SA, Smith J, Mahran A, Fox P, Fakis A. Double-blind randomized controlled trial of letrozole versus clomiphene citrate in women with polycystic ovary syndrome. *Hum Reprod*. 2017;32(8):1631–8.
7. Morley LC, Tang T, Yasmin E, Norman RJ, Balen AH. Insulin-sensitising drugs in PCOS. *Cochrane Database Syst Rev*. 2017;11:CD003053.
8. Tang T, Lord JM, Norman RJ, Yasmin E, Balen AH. Insulin-sensitising drugs for women with polycystic ovary syndrome. *Cochrane Database Syst Rev*. 2012;5:CD003053.
9. Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for PCOS. *Hum Reprod*. 2018;33(9):1602–18.
10. Wang R, Kim BV, van Wely M, et al. Treatment strategies for women with WHO group II anovulation. *Hum Reprod*

Update. 2017;23(6):687–708.
11. McCartney CR, Marshall JC. Clinical practice: PCOS. *N Engl J Med*. 2016;375:54–64.
12. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised consensus on PCOS. *Hum Reprod*. 2004;19(1):41–7.
13. Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson P, et al. Letrozole versus clomiphene for infertility in PCOS. *N Engl J Med*. 2014;371(2):119–29.
14. Costello MF, Misso ML, Balen A, et al. Evidence summaries for PCOS guideline. *Hum Reprod Open*. 2019;2019(1):hoy021.
15. Goodman N, Cobin RH, Futterweit W, et al. AACE PCOS guidelines. *Endocr Pract*. 2015;21(11):1291–1300.