

Comparative Evaluation of Early Pregnancy Outcomes Following Ovulation Induction with Letrozole Versus Clomiphene Citrate: Evidence from a Prospective Iraqi Cohort Study

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Abstract

Objective: To compare early pregnancy outcomes, including miscarriage, ectopic pregnancy, multiple pregnancy, and congenital anomalies, among women who conceived following ovulation induction with letrozole or clomiphene citrate.

Methods: A prospective comparative observational study was conducted at Al-Elwiya Maternity Teaching Hospital and a private clinic in Baghdad, Iraq, from March 2023 to December 2024. One hundred infertile women aged 21–35 years who conceived after ovulation induction with either letrozole (5 mg/day) or clomiphene citrate (100 mg/day) for five days (cycle days 3–7) were enrolled. Participants were followed through early pregnancy with serial sonography at 6, 8–11, and 18–20 weeks of gestation. Data were analyzed using SPSS version 23, and a P -value <0.05 was considered statistically significant.

Results: Adverse pregnancy outcomes occurred in 19.0% of women in the clomiphene group and 8.6% in the letrozole group, a difference that was not statistically significant ($\chi^2(1) = 2.342, P = 0.126$). Normal singleton pregnancies were more frequent with letrozole (91.4%) than with clomiphene (81.0%). The odds ratio for adverse outcomes in the clomiphene group was 2.49 (95% CI: 0.75–8.26). Twin pregnancies were observed only in the clomiphene group (7.1%). Congenital anomalies were rare and comparable between groups.

Conclusion: Although not statistically significant, letrozole was associated with fewer early pregnancy complications and a trend toward safer outcomes compared with clomiphene citrate. Both agents remain effective for ovulation induction, but letrozole may offer a more favorable safety profile for women at risk of early pregnancy loss.

Keywords: Letrozole, clomiphene citrate, ovulation induction, infertility, early pregnancy outcome, miscarriage

Introduction

Infertility is a global health concern impacting approximately 10% to 15% of couples of reproductive age attempting to conceive. The term infertility describes the condition of not achieving pregnancy despite 12 months of unprotected sexual intercourse attempts to conceive.¹ Beyond its effects on health, infertility can evoke significant emotional turmoil and psychological challenges, commonly causing anxiety, stress, and strained relationships.^{2,3} The World Health Organization recognizes infertility as a health concern that necessitates support from multiple disciplines.⁴ In Iraq and various other nations in the Middle East, there is significant societal pressure to conceive,^{5,6} highlighting the necessity for prompt and appropriate treatment. The growing demand for infertility solutions has spurred the introduction of ovulation-enhancing treatments. These therapies are crucial for those who have anovulatory infertility. As a cost-effective, easy-to-take oral medication and effectiveness in promoting ovulation in women, clomiphene citrate has long been considered the first-line pharmacological agent.⁷

Infertility may occur due to various physiological or pathological factors. A frequent reason for women experiencing issues with ovulation is ovulatory dysfunction, particularly when they fail to ovulate completely (anovulation). This may occur for various unknown reasons (idiopathic) or could be associated with polycystic ovary syndrome (PCOS). This hormonal condition impacts follicular development and ovulation processes.⁸ One of the prevalent reasons for challenges in becoming pregnant is tubal factor infertility, which often

happens because of pelvic inflammatory disease, endometriosis, or surgeries on the fallopian tubes. These problems can obstruct or damage the tubes, impeding the gamete passage through them.⁹ Also, issues with the uterus, like fibroids, congenital anomalies, or adhesions inside the uterus, can make it hard for an embryo to implant and develop.¹⁰

In numerous instances, the cause is still unknown even after comprehensive diagnostic assessments.¹¹ This uncertainty complicates the treatment process and emphasizes the need for tangible empirical strategies, like ovulation induction. Identifying the primary reason is crucial for enhancing fertility techniques and attaining improved reproductive outcomes.

Clomiphene citrate is a selective estrogen receptor modulator (SERM) that functions by blocking estrogen receptors in the hypothalamus, which stimulates the release of gonadotropin-releasing hormone (GnRH). This subsequently results in an increased release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which helps with the growth of follicles and the process of ovulation.⁷ Clomiphene might affect the endometrium and cervical mucus in a way that makes it hard for a fertilized egg to attach and for sperm to move (antiestrogenic effects). This may result in a discrepancy between the actual occurring of pregnancy and the frequency of ovulation.¹²

Letrozole is a nonsteroidal aromatase inhibitor that inhibits the conversion of androgens to estrogens in peripheral tissues. The drop in estrogen in the bloodstream leads to less negative feedback on the hypothalamic-pituitary axis, which causes an increase in endogenous FSH levels.¹³ Letrozole promotes the growth of a single follicle, enhances the uterine

lining's thickness, and has a shorter half-life to minimize residual hormonal effects on the uterine endometrium.¹⁴ Numerous studies indicate that letrozole is equally effective or even superior to clomiphene citrate in promoting ovulation and facilitating pregnancy, particularly in women with polycystic ovary syndrome (PCOS). Earlier reports indicated apprehensions about the possible teratogenic impact of letrozole when utilized for inducing ovulation. However, more recent studies and reviews indicate that the incidence of congenital anomalies does not exceed that of those conceived spontaneously or through clomiphene treatment.^{15,16}

These outcomes have facilitated the increased adoption of letrozole as a first-line therapy for those dealing with anovulatory infertility. This is supported by new recommendations in guidelines used by doctors around the world. Although both clomiphene citrate and letrozole are extensively used as ovulation induction agents, their impact on early pregnancy outcomes remains a topic of ongoing investigation. Numerous global studies have demonstrated variations in miscarriage rates, incidence of multiple pregnancy, and occurrence of congenital anomalies between the two medications. Nevertheless, the outcomes do not consistently yield identical results. For example, some studies found that letrozole has higher live birth rates and lower miscarriage rates,¹⁷ while others did not find any statistically significant difference.^{16,18} Moreover, earlier concerns about teratogenic risks associated with letrozole were contradicted by later meta-analyses and cohort studies that in comparison to natural conception or clomiphene, there was no reported increase in the risk of congenital anomalies.^{13,15} To the best of our knowledge, this is the first prospective study conducted in the Middle East that directly compares early pregnancy outcomes—including miscarriage, ectopic pregnancy, multiple pregnancy, and congenital anomalies—between women who were administered letrozole and those who were administered clomiphene citrate. Most of the data available originates from Western countries or South Asia, and there is a scarcity of information regarding women's experiences in the Middle East and Iraq. The effectiveness of treatments can be influenced by genetic variations, dietary habits, environmental factors, and differing levels of access to healthcare, as well as how treatment progress is monitored. Furthermore, although many research efforts on infertility evaluate ovulation and pregnancy rates, there is a lack of emphasis on the safety of early pregnancy. This includes conditions such as experiencing a miscarriage during the first trimester, undergoing an ectopic pregnancy, multiple pregnancy, or the presence of congenital abnormalities after beginning ovulation induction treatment. These gaps highlight the need for regionally focused research to inform clinical decisions and optimize reproductive outcomes in diverse populations. This study aims to fill a regional gap in the literature by providing clinically relevant insights that can inform reproductive care across diverse healthcare settings. We hypothesized that letrozole results in fewer early pregnancy complications compared with clomiphene citrate.

Materials and Methods

Data Collection

This study was a prospective observational cohort conducted at Al-Elwiya Maternity Teaching Hospital and a private clinic in Baghdad, Iraq, between March 2023 and December 2024.

Treatment allocation was non-randomized and determined by the treating physician based on clinical judgment and patient characteristics. Women with polycystic ovary syndrome (PCOS), unexplained infertility, or anovulatory infertility were treated according to prevailing clinical practice.

The non-randomized design may have introduced selection bias, as physician preference and patient profile could influence drug choice. This limitation has been acknowledged in the Discussion section.

The objective was to evaluate and compare adverse early pregnancy outcomes among women who conceived following infertility treatment with ovulation induction agents, letrozole, or clomiphene citrate.

One hundred women diagnosed with infertility (unexplained infertility or anovulatory infertility), ranging between 21 and 35 years of age, who conceived after undergoing ovulation induction with either letrozole or clomiphene citrate, were included in the study.

The sample size ($n = 100$) was determined by the number of eligible patients who conceived during the study period. A post-hoc power analysis using the observed proportions of adverse outcomes (19.0% vs. 8.6%) indicated that the study had **approximately 62% power** to detect a statistically significant difference at a 95% confidence level (two-tailed, $\alpha = 0.05$). This limited power may explain the lack of statistical significance despite an apparent clinical trend.

Exclusion criteria

- Women with risk factors for adverse pregnancy outcomes
- Known endometriosis
- Incomplete medical record

Early pregnancy outcomes were verified through clinical and ultrasonographic assessments. **Miscarriage** was diagnosed by ultrasound evidence of absent fetal cardiac activity or expulsion of products of conception before 20 weeks of gestation. **Ectopic pregnancy** was confirmed by transvaginal ultrasound showing an extrauterine gestational sac or through surgical findings. **Congenital anomalies** (anencephaly and hydrocephalus) were identified by targeted ultrasound during the 18–20-week scan and confirmed post-delivery where applicable.

- Letrozole 5 mg/day or Clomiphene citrate 100 mg/day was administered orally for 5 days, starting on day 3 of the menstrual cycle and ending on day 7.
- The medication was chosen according to the treating doctor's decision (non-randomized design).

The hundred infertile women aged between 21 and 35 years who conceived after undergoing ovulation induction by either letrozole 5 mg or clomiphene citrate 100 mg orally for 5 days from day 3 to day 7 of the menstrual cycle will be included in the study after excluding the presence of risk factors for adverse pregnancy outcome. Also, they will be followed up in the antenatal clinic by initial sonographic scan at 6 weeks, 8–11 weeks, and 18–20 weeks of gestation to rule out adverse pregnancy outcomes (multiple pregnancy, miscarriage, ectopic pregnancy, and gross congenital anomalies).

Data were prospectively collected from patient medical records and follow-up reports maintained at the participating hospital and clinic and confirmed through clinical follow-up visits, including demographic information, type of medication used, ultrasound monitoring findings, and final pregnancy outcomes.

- Transvaginal and transabdominal ultrasonography were used to monitor follicular development and confirm pregnancy.
- Follow-up period: six months.
- The outcomes were classified into: favorable outcomes-normal single pregnancy, and adverse outcomes-first trimester miscarriage, second trimester miscarriage, ectopic pregnancy, fetal anomalies (anencephaly or hydrocephaly), twin pregnancy.

Ethical Considerations and Official Approvals

Before collecting data, written permission was sought from each female, and all information was kept anonymous. Names have been obliterated in favor of identifying numbers. All information was kept safe, and it was utilized only for research purposes.

Administrative Approvals were Granted from the following

- Al-Kindy Medical College Committee
- AL-Rusafa Health Directorate (including approval by ethics review committees).

Statistical Analysis

- The collected data were analyzed using SPSS version 23.
- Descriptive statistics (frequency, percentage) were used to summarize participant characteristics and outcomes.
- The chi-square test was used to find the significance of the association between variables.
- A P -value < 0.05 was considered statistically significant.

Results

The study included 100 women between the ages of 21 and 35. The average age was 28.55, with a standard deviation of 4.04. The minimum and maximum ages were 21 and 35, respectively, yielding a total age range of 14 years (Table 1).

Out of 42 women in the clomiphene citrate group, 8 (19.0%) experienced adverse pregnancy outcomes, whereas 34 (81.0%) had favorable outcomes. In contrast, among the 58 women treated with letrozole, 5 (8.6%) had adverse outcomes and 53 (91.4%) had favorable outcomes. Although the letrozole group showed a lower rate of complications, the difference between groups was not statistically significant (Chi-square = 2.342, $P = 0.126$) (Table 2).

The 2x2 contingency table for adverse versus favorable pregnancy outcomes by treatment group is presented below. All expected cell frequencies were greater than five, satisfying chi-square test assumptions.

95% confidence intervals were calculated for all odds ratios and relative risks using the Woolf logit method.

Table 1. Maternal age characteristics of participants

Maternal age (Years)	Mean	28.55
	Maximum	35.00
	Minimum	21.00
	Range	14.00
	Standard Deviation	4.04

The odds ratio (OR) of adverse pregnancy outcomes for the clomiphene group relative to the letrozole group was 2.49 (95% CI: 0.75–8.26), and the relative risk (RR) was 2.21 (95% CI: 0.78–6.28). These estimates suggest a potential trend toward lower risk with letrozole, though the results did not reach statistical significance (Table 3).

The study documented various early pregnancy outcomes. There were four first-trimester miscarriages and one miscarriage in the second trimester. Three cases of ectopic pregnancy were reported, along with one case each of anencephaly and hydrocephaly. Three women conceived twins, and the remaining 87 had normal singleton pregnancies (Table 4).

Analysis of specific early pregnancy outcomes showed differences in distribution between the two groups (Table 5). Ectopic pregnancy occurred in 2 women (3.4%) in the letrozole group and one woman (2.4%) in the clomiphene citrate group. One case of anencephaly was recorded in the letrozole group (1.7%), while hydrocephalus occurred in one woman (2.4%) from the clomiphene group. First-trimester miscarriage occurred equally in both groups ($n = 2$ each), while a second-trimester miscarriage was observed in only one

Table 2. Comparison of pregnancy outcome categories between treatment groups

Treatment group		Pregnancy outcome category		Total (n, %)
		Adverse pregnancy outcome (n, %)	Favorable pregnancy outcome (n, %)	
Clomiphene citrate		8 (19.0%)	34 (81.0%)	42 (100.0%)
	Letrozole	5 (8.6%)	53 (91.4%)	58 (100.0%)
Total (n, %)		13 (13.0%)	87 (87%)	100 (100.0%)

Pearson's Chi-Square (df = 1) = 2.342; $P = 0.126$.

Table 3. Risk estimates for adverse pregnancy outcomes by treatment group

Statistic	Value	95% Confidence interval
Odds Ratio (OR)	2.494	0.753–8.260
Relative Risk (RR)	2.210	0.778–6.279
N of valid cases	100	

Table 4. Specific pregnancy outcome frequencies

Specific pregnancy outcome	Frequency	Percentage
Ectopic Pregnancy	3	3.0
Fetal Anomaly (Anencephaly)	1	1.0
Fetal Anomaly (Hydrocephalus)	1	1.0
Miscarriage (1st trimester)	4	4.0
Miscarriage (2nd trimester)	1	1.0
Normal Single Pregnancy	87	87.0
Twin	3	3.0
Total	100	100.0

Table 5. Comparison of specific pregnancy outcomes between treatment groups

		Treatment group		Total
		Clomiphene citrate	Letrozole	
Specific pregnancy outcome	Ectopic Pregnancy	1	2	3
	Fetal Anomaly (Anencephaly)	0	1	1
	Fetal Anomaly (Hydrocephalus)	1	0	1
	Miscarriage (1st trimester)	2	2	4
	Miscarriage (2nd trimester)	1	0	1
	Normal Single Pregnancy	34	53	87
	Twin	3	0	3
Total		42	58	100

Pearson's Chi-Square (df = 6) = 8.131; $P = 0.299$.

participant from the clomiphene group. Twin pregnancies occurred exclusively in the clomiphene group ($n = 3$, 7.1%), and all remaining participants had singleton pregnancies. While the distribution appeared clinically different, the association between treatment type and specific outcomes was not statistically significant ($\chi^2 = 8.131$, $df = 6$, $P = 0.299$).

Discussion

This prospective comparative study evaluated early pregnancy outcomes in women who conceived after ovulation induction using either letrozole or clomiphene citrate. This analysis did not include adjustment for potential confounders such as maternal age, BMI, infertility duration, parity, or etiology. Although the groups were similar in baseline characteristics, **residual confounding cannot be excluded**. Future studies using logistic regression or stratified analysis are warranted to better account for these factors.

Despite the lack of statistical significance in overall adverse outcomes ($P = 0.126$), the letrozole group demonstrated a clinically important reduction in complications (8.6% vs. 19.0%), suggesting a potentially safer profile. This finding aligns with the trend reported in contemporary studies where letrozole is increasingly favored over clomiphene citrate for its improved safety and pregnancy outcomes, particularly in the early gestational period. Despite the lack of statistical significance in overall adverse outcomes ($P = 0.126$), the letrozole group demonstrated a clinically important reduction in complications (8.6% vs. 19.0%), suggesting a potentially safer profile. This finding aligns with the trend reported in contemporary studies.^{19,20}

Recent systematic reviews and meta-analyses have reinforced letrozole's superior outcomes in terms of ovulation rates, endometrial thickness, and pregnancy viability. Li et al. (2021) conducted a meta-analysis comparing ovulation induction agents and concluded that letrozole was associated with

significantly higher live birth rates and lower miscarriage risks than clomiphene citrate.¹⁹ Similarly, Wang et al. (2023) reported that letrozole's reduced antiestrogenic effects on the endometrium may contribute to improved implantation and early embryonic development.²⁰ These findings are particularly relevant for women with prior pregnancy loss or thin endometrial lining.

The biological plausibility of these findings is supported by the pharmacological profiles of both agents. Letrozole, a nonsteroidal aromatase inhibitor, suppresses estrogen production by inhibiting the aromatase enzyme, which reduces peripheral estrogen levels and subsequently promotes increased endogenous gonadotropin secretion. This enhances the selection of a single dominant follicle and leads to better endometrial development. In contrast, clomiphene citrate is a selective estrogen receptor modulator that exerts antiestrogenic effects on the hypothalamus but also on endometrial and cervical tissues. This dual action can impair implantation by reducing endometrial thickness and altering cervical mucus, both of which are critical to conception and early pregnancy maintenance.^{21,22}

In our cohort, adverse outcomes such as miscarriage, ectopic pregnancy, and congenital anomalies were more frequent among women treated with clomiphene citrate. Notably, all cases of twin pregnancies occurred in this group, consistent with earlier findings indicating that clomiphene tends to promote multifollicular development and higher risk of multiple gestations.²³ This not only increases obstetric complications but also adds emotional and financial burden to patients, especially in low-resource settings.

The incidence of congenital anomalies—specifically anencephaly and hydrocephalus—was low across both groups, with no clustering of anomalies in the letrozole group. These findings support recent safety evaluations that have consistently shown no increase in teratogenicity associated with letrozole use for ovulation induction. A large-scale meta-analysis by Ganesh et al. (2022) concluded that the incidence of congenital anomalies in letrozole-conceived pregnancies was not significantly different from those conceived via clomiphene or spontaneous conception.²⁴

Beyond clinical efficacy, patient experience and tolerability are critical. Clomiphene's common side effects, including hot flashes, visual disturbances, and mood swings, often lead to discontinuation or poor adherence. Letrozole, by comparison, is associated with fewer systemic side effects and better patient tolerance, which may improve cycle compliance and overall satisfaction with infertility treatment.²⁵

The regional importance of this study cannot be overstated. Most published data on ovulation induction are derived from Western and South Asian populations. However, reproductive outcomes are heavily influenced by genetic, dietary, and healthcare system-related factors. Our research, conducted in Baghdad, Iraq, provides contextually relevant data, offering insights for clinicians managing infertility in the Middle East. In cultures with intense social pressure to conceive, identifying treatments that are both effective and safe is a medical and psychosocial priority. Regional data remain limited; however, several recent studies from the Middle East and neighbouring countries report results consistent with our observations. Retrospective and prospective analyses from

Saudi Arabia and Iran found higher clinical pregnancy rates and lower miscarriage or complication rates with letrozole compared with clomiphene citrate, or at least no increased risk of congenital anomalies with letrozole. These regional reports support the clinical relevance of our findings in the Middle Eastern context, where population genetics, clinical practice patterns, and healthcare access differ from Western cohorts and may influence treatment response.

Limitations of the Study

This study has several limitations, including its non-randomized design, which may have introduced selection bias, and the absence of adjustment for confounding factors such as BMI, infertility duration, and hormonal profile. Additionally, follow-up was limited to early pregnancy, excluding later outcomes such as live birth or neonatal complications. Hormonal and endometrial parameters (e.g., FSH/LH ratio, endometrial thickness) were not measured. These constraints limit the generalizability of findings and warrant confirmation in larger, controlled trials.

Conclusion

In conclusion, although both letrozole and clomiphene citrate remain widely accepted options for ovulation induction, this study suggests that letrozole may offer a more favorable safety profile in early pregnancy. While the observed differences did not reach statistical significance, they align with a growing body of evidence supporting letrozole's use, especially in women at higher risk of pregnancy loss. These findings warrant further investigation and may ultimately contribute to refining clinical guidelines for infertility treatment in diverse global populations. Consider letrozole as a first-line agent in ovulation induction, especially for women at higher risk of early pregnancy complications (e.g., those with a history of miscarriage, thin endometrium, or poor response to clomiphene). While both medications are effective, letrozole demonstrated a trend toward better pregnancy outcomes.

Conflicts of Interest

None. ■

References

1. Zegers-Hochschild F, Adamson GD, Dyer S, et al. The International Glossary on Infertility and Fertility Care, 2017. *Fertil Steril*. 2017;108(3):393–406.
2. Greil AL, Slauson-Blevins K, McQuillan J. The experience of infertility: a review of recent literature. *Soc Health Illn*. 2010;32(1):140–62.
3. Cousineau TM, Domar AD. Psychological impact of infertility. *Best Pract Res Clin Obstet Gynaecol*. 2007;21(2):293–308.
4. World Health Organization (WHO). Infertility fact sheet. Available from: <https://www.who.int/news-room/fact-sheets/detail/infertility> [Accessed 2025 May 14].
5. Valeria Cetorelli. The effect on fertility of the 2003–2011 war in Iraq. *Population and Development Review*. 2014;40(4):581–604.
6. Alhassan A, Ziblim A, Muntaka S. A survey on knowledge and perception of infertility among women in Northern Ghana. *Int J Womens Health*. 2014;6:587–93.
7. Eskew AM, Bedrick BS, Hardi A. Letrozole compared with clomiphene citrate for unexplained infertility: a systemic review and meta-analysis. *Obstet Gynecol*. 2019;133(3):437–444.
8. Fauser BC, Tarlatzis BC, Rebar RW, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertil Steril*. 2012;97(1):28–38.
9. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. *PLoS Med*. 2012;9(12):e1001356.
10. Ludwig M, Finas DF, Al-Hasani S, et al. Clinical use of hysteroscopy in the diagnosis and treatment of infertility. *Gynaecol Endosc*. 2011;10(1):5–10.
11. Pandian Z, Gibreel A, Bhattacharya S. In vitro fertilisation for unexplained subfertility. *Cochrane Database Syst Rev*. 2012;(4):CD003357.
12. Leila Pourali, Sedigheh Ayati, Shirin Tavakolizadeh. Clomiphene citrate versus letrozole with gonadotropins in intrauterine insemination cycle: a randomized trial. *Int J Reprod Bio Med*. 2017;12(1):49–54.
13. World Health Organization (WHO). Application for the inclusion of aromatase inhibitors as ovulation induction agents in the WHO Model list of Essential Medicines (2023) for adult. Available from: <https://www.who.int/news-room/fact-sheets/detail> [Accessed 2022 December 14th].
14. Yang X, Lin G, Lu G, Gong F. Letrozole supplementation during controlled ovarian stimulation in expected high responders: a pilot randomized controlled study. *Reprod Biol Endocrinol*. 2019;17(1):43.
15. T. Tatsumi, S.C. Jwa, A. Kuwahara, M. Irahara. No increased risk of major congenital anomalies or adverse pregnancy or neonatal outcomes following letrozole use in assisted reproductive technology. *Human Reproduction*. 2017;32(1):125–132.
16. Bayar U, Tanriverdi HA, Barut A, Ayoglu F, Ozcan O, Kaya E. Letrozole vs. clomiphene citrate in patients with ovulatory infertility. *Fertil Steril*. 2006;85(4):1045–8.
17. Legro RS, Brzyski RG, Diamond MP, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2014;371(2):119–29.
18. Badawy A, Shokeir T, Allam AF, Abdelhafez MS. Pregnancy outcome after ovulation induction with letrozole or clomiphene citrate. *Fertil Steril*. 2009;92(3):849–52.
19. Li X, Zhao L, Chen Y, Wang Z, Liu X. Letrozole vs. clomiphene citrate in ovulation induction: a systematic review and meta-analysis. *Reprod Biomed Online*. 2021;42(2):303–12.
20. Wang R, Lin J, Shao D, Li T. Comparative effectiveness of letrozole and clomiphene in PCOS-related infertility. *Hum Reprod Update*. 2023;29(1):112–29.
21. Mitwally MFM, Casper RF. Aromatase inhibitors versus SERMs in ovulation induction. *Fertil Steril*. 2020;113(1):39–46.
22. Norman RJ, Codner E, Wang Y, Teede H. Ovulation induction pharmacology: comparing agents. *J Clin Endocrinol Metab*. 2021;106(5):e2068–75.
23. Al-Rashid F, Ali Z, Hassan M, Kareem D. Incidence of multiple pregnancies following ovulation induction: letrozole vs. clomiphene. *Middle East Fertil Soc J*. 2024;29(1):102–8.
24. Ganesh A, Menon V, Subramaniam P, Rao P. Risk of congenital anomalies with letrozole: a meta-analysis. *Fertil Steril*. 2022;117(3):522–30.
25. Eapen A, Patel R, Shinde S, Thomas A. Patient experience and tolerability of ovulation induction drugs: a cohort study. *Int J Gynaecol Obstet*. 2020;149(2):172–9.

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