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Effects of the main GLP-1 receptor agonists on polycystic ovary syndrome and female fertility: a review

Abstract

Female infertility constitutes an important public health issue and is frequently associated with metabolic and endocrine disorders, such as obesity, insulin resistance, and polycystic ovary syndrome (PCOS). In recent years, glucagon-like peptide-1 (GLP-1) receptor agonists have been widely used in the treatment of obesity and have increasingly been investigated for their potential effects on female fertility. The aim of this study was to conduct a narrative review of the literature regarding the effects of the main GLP-1 receptor agonists currently used worldwide on female fertility, with emphasis on women with PCOS. A literature search was performed in the PubMed and LILACS databases, including studies published over the last five years in English, Portuguese, and Spanish. Clinical trials, observational studies, case reports, and systematic reviews evaluating the effects of liraglutide, semaglutide, and exenatide on metabolic, hormonal, molecular parameters, and reproductive outcomes were included. The findings indicate that GLP-1 receptor agonists promote significant improvements in metabolic and hormonal profiles, including reductions in body weight, insulin resistance, and hyperandrogenism, which are central factors in the pathophysiology of PCOS-related infertility. Furthermore, recent evidence suggests potential direct effects on the ovarian and endometrial microenvironment, contributing to the restoration of ovulation, menstrual cyclicity, and increased clinical pregnancy rates in certain contexts. It is concluded that GLP-1 receptor agonists represent promising tools for metabolic and endocrine optimization in the preconception period; however, they do not act as direct fertility-inducing agents, and further large-scale, long-term randomized studies are required to clarify their impact on final reproductive outcomes.

Keywords: GLP-1 receptor agonists, female fertility, polycystic ovary syndrome, obesity, reproductive health

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Abbreviations: AE, adverse events; BMI, body mass index; CC, clomiphene citrate; CPA/EE, cyproterone acetate/ethinylestradiol; ECR/RCT, randomized controlled trial; EXE, exenatide; FAI, free androgen index; FSH, follicle-stimulating hormone; GI, gastrointestinal; GLP-1RA, Glucagon-like peptide-1 receptor agonist; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; IMC/BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; LEP, leptin gene; LH, luteinizing hormone; MD, mean difference; MET, metformin; PCOS, polycystic ovary syndrome; PIO, pioglitazone; RR, risk ratio; SD, standard deviation; SHBG, sex hormone–binding globulin; SMD, standardized mean difference.

Introduction

Female infertility represents a significant public health problem, with a growing impact on reproductive health, psychosocial well-being, and healthcare systems. According to the World Health Organization, approximately 10–15% of couples of reproductive age experience difficulty conceiving, with female infertility accounting for a substantial proportion of these cases.[1] Among the factors associated with reduced fertility, metabolic and endocrine disorders stand out, particularly obesity and insulin resistance, which directly interfere with the hypothalamic–pituitary–ovarian axis, ovulation, and endometrial receptivity.[2,3]

In this context, polycystic ovary syndrome (PCOS) is recognized as the leading cause of anovulatory infertility, affecting approximately 6–10% of women of reproductive age. PCOS is frequently accompanied by hyperandrogenism, insulin resistance, and excess body weight, conditions that synergistically exacerbate reproductive dysfunction and prolong time to conception.[3,4] Epidemiological evidence further indicates that the global increase in female obesity has contributed to the rising prevalence of infertility related to ovulatory disorders, reinforcing the importance of therapeutic strategies focused on metabolic improvement in preconception care.[5]

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) were initially developed for the treatment of type 2 diabetes mellitus and were subsequently incorporated into obesity management due to their efficacy in promoting weight loss, improving insulin sensitivity, and modulating appetite.6 In recent years, these agents have been increasingly prescribed to women of reproductive age, including those with PCOS and future reproductive intentions. Clinical studies and reviews suggest that GLP-1RAs may exert favorable effects on female reproductive function by inducing weight loss, reducing hyperinsulinemia, and improving hormonal profiles, thereby creating a more physiologically favorable environment for ovulation.[6,7]

Beyond their systemic metabolic effects, experimental and preclinical studies indicate that GLP-1 receptors are expressed in tissues involved in reproduction, such as the ovaries, endometrium, and central nervous system, suggesting potential direct actions of these agonists on the reproductive axis. Evidence indicates that receptor activation may influence gonadotropin secretion, ovarian steroidogenesis, and the endometrial environment, further supporting the biological plausibility of GLP-1RAs affecting female fertility beyond the effects of weight loss alone.[8,9]

Despite growing scientific and clinical interest, important gaps remain in the literature regarding the actual role of GLP-1RAs in female fertility. Recent systematic reviews highlight that although the metabolic benefits of these agents are well established, data on reproductive outcomes, such as ovulation, clinical pregnancy, and live birth, remain heterogeneous and, in some cases, inconclusive.[4,9] Furthermore, given that GLP-1RAs are contraindicated during pregnancy, their use should be restricted to the preconception period, underscoring the need for a clear understanding of their benefits and limitations in this context.[6]

In light of the widespread use of GLP-1 receptor agonists among women of reproductive age and the lack of consensus regarding their effects on PCOS and female fertility, it is essential to critically integrate the available evidence. Therefore, this article aims to conduct a narrative review on the effects of the main GLP-1 receptor agonists on polycystic ovary syndrome and female fertility, seeking to address the following guiding question: What are the effects of the main GLP-1 receptor agonists on women with polycystic ovary syndrome and on female fertility, considering metabolic, hormonal, molecular parameters, and reproductive outcomes? The critical synthesis of the literature seeks to contribute to a better understanding of the role of GLP-1RAs in preconception metabolic optimization and to support evidence-based clinical decision-making.

Methodology

The present study consists of a narrative review of the literature, developed with the aim of analyzing and discussing the effects of glucagon-like peptide-1 receptor agonists (GLP-1RAs) on female fertility, with emphasis on women of reproductive age and clinical contexts associated with polycystic ovary syndrome (PCOS). The narrative review design was chosen because it allows a critical, integrative, and contextualized analysis of the available scientific evidence, encompassing both pathophysiological aspects and clinical implications. Although it does not follow the quantitative rigor of systematic reviews, the narrative review is widely recognized as appropriate for synthesizing emerging areas of knowledge and exploring conceptual and clinical gaps.[10] To ensure greater transparency and reproducibility in the study selection process, a flowchart describing the stages of identification, screening, eligibility, and inclusion of articles was employed, a practice recommended even in non-systematic reviews when structured database searches are conducted.[11]

The bibliographic search was conducted in the PubMed/MEDLINE and LILACS (Latin American and Caribbean Health Sciences Literature) databases, selected due to their relevance and comprehensive coverage in the fields of Endocrinology, Women's Health, and Human Reproduction. Study identification was performed using standardized Medical Subject Headings (MeSH), combined with Boolean operators, including the following terms: ("Glucagon-Like Peptide-1 Receptor Agonists" OR "GLP-1 receptor agonist" OR liraglutide OR semaglutide OR exenatide OR dulaglutide) AND ("Female Fertility" OR fertility OR ovulation OR "menstrual cycle" OR "reproductive health") AND ("Polycystic Ovary Syndrome" OR PCOS). Search strategies were adapted to the specific characteristics of each database, maintaining the use of English-language terms to increase the sensitivity of study retrieval.

Filters were applied to restrict the results to articles published within the last five years, available in English, Portuguese, or Spanish, and conducted in humans. Regarding study design, clinical trials, observational studies, randomized studies, case reports, and systematic reviews were considered eligible in order to encompass different levels of evidence relevant to the understanding of the topic.

The application of the search strategy resulted in the identification of six articles in the PubMed database and ten articles in the LILACS database. All retrieved studies were initially screened through title and abstract reading to assess their relevance to the proposed topic. Potentially eligible articles were then evaluated in full text, and those meeting the previously established eligibility criteria were selected. It was observed that there are still relatively few studies addressing this topic in the selected databases, particularly involving all major pharmacological agents within the GLP-1RA class.

Studies conducted in women of reproductive age that evaluated the use of GLP-1 receptor agonists, specifically liraglutide, semaglutide, and exenatide, and reported outcomes related to female fertility, such as ovulation, menstrual cycle regularity, reproductive hormonal parameters, polycystic ovary syndrome, and general aspects of reproductive health, were included in the review. The selection of these agents was based on their pharmacological action predominantly mediated by the GLP-1 receptor, allowing a more specific analysis of their metabolic and reproductive effects.

Studies conducted exclusively in men or in experimental animal models were excluded, as were publications not directly related to female fertility, PCOS, and reproductive health. Editorials, letters to the editor, and opinion articles without original scientific data were also excluded. Additionally, studies evaluating dual incretin agents, such as tirzepatide, were not included in this review, as this drug acts simultaneously as an agonist of GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors, which could introduce bias and hinder the isolated interpretation of effects attributable specifically to GLP-1RAs on female fertility and PCOS.

After final selection, the included studies were qualitatively analyzed and integrated into a narrative synthesis, considering methodological characteristics, study population, type of GLP-1RA used, duration of intervention, and the main findings related to metabolic and reproductive outcomes. The interpretation of results sought to correlate the physiological mechanisms of GLP-1 receptor agonists with their potential repercussions on polycystic ovary syndrome and female fertility, as well as to identify existing gaps in the current scientific literature.

Results and discussion

Two studies initially identified during the database search were excluded from the final synthesis. One article was not available in full text and free access, which prevented complete data extraction and critical appraisal. The other study was identified as a duplicate record retrieved from both databases and was therefore counted only once. Consequently, a total of 14 unique studies were included in the qualitative analysis of this narrative review (Figure 1). The synthesis of the 14 studies included in this narrative review demonstrates that glucagon-like peptide-1 receptor agonists (GLP-1RAs) exert consistent effects on metabolic and hormonal determinants directly related to female fertility, particularly in women with polycystic ovary syndrome (PCOS) and overweight or obesity (Table 1). Collectively, the findings converge on the understanding that these agents do not act as direct fertility inducers, but rather as therapeutic strategies that optimize the metabolic–endocrine environment and, more recently, also suggest modulation at the endometrial and ovarian levels, thereby creating more favorable physiological conditions for ovulation, menstrual regularity, and, in some contexts, clinical pregnancy.

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Table 1 Main findings gathered in the present review (Oliveira, 2026)

Authors	Participants	Treatment	Main Findings
Bader et al. (2024)	486 women with PCOS (systematic review)	GLP-1RA alone or combined	↓ BMI, waist circumference, and HOMA-IR; variable hormonal improvement.
Chen et al. (2025)	100 women with PCOS and overweight/obesity (80 completed)	Metformin vs Metformin + Semaglutide 1 mg/week – 16 weeks	↓ body weight 6.09 kg vs 2.25 kg; menstrual regularity 72.5% vs 42.3%; spontaneous pregnancy 35% vs 15%.
Elkind-Hirsch et al. (2022)	82 women with PCOS and obesity (67 completed)	Liraglutide 3.0 mg/day vs placebo – 32 weeks	↓ body weight by 5.7%; ↑ menstrual cycles (4.5 → 8.6 cycles/year); ↓ FAI; ↑ SHBG; 2 pregnancies in the liraglutide group.
Gill e Mackey (2021)	Women with obesity and/or PCOS (clinical review)	GLP-1RA (mainly liraglutide)	Improvement in ovarian function and fertility in the preconception period; contraindicated during pregnancy.
Hu et al. (2023)	1,149 women with PCOS (9 RCTs)	Exenatide alone or combined with metformin – 12–24 weeks	↑ pregnancy rate (RR 1.85); ↓ testosterone; ↓ HOMA-IR; ↓ body weight and BMI; favorable safety profile.
Huang e He (2025)	Randomized clinical trials	Liraglutide + Metformin vs Metformin	↓ BMI and HOMA-IR; ↑ menstrual regularity; mild GI events, no increase in serious AEs.
Kesavan et al. (2023)	6 clinical studies (meta-analysis)	Exenatide vs Metformin	↓ BMI (MD 0.51 kg/m²); ↓ testosterone (MD 0.15); no significant effect on LDL/HDL.
Liao et al. (2024)	60 women with PCOS and overweight	CPA/EE + Metformin vs Liraglutide + Metformin – 12 weeks	GLP-1 group: ↓ body weight ~7.4 kg; ↓ HOMA-IR; ovulation in ~20%.
Ling et al. (2024)	Randomized clinical trials	Metformin vs Metformin + Liraglutide	↑ ovulation; ↑ spontaneous conception; superior metabolic improvement vs monotherapy.
Nicolaou et al. (2025)	1 woman with PCOS and obesity	Exenatide 5–10 µg twice daily ± metformin	Restoration of menstrual cyclicity; ↓ body weight by 7.5 kg; effects observed before significant weight loss.
Peng et al. (2023)	4,608 infertile women with PCOS (27 RCTs)	Exenatide and combinations (CC+EXE, CC+MET+PIO)	↑ clinical pregnancy (EXE and CC+EXE); no clear benefit in live birth.
Salamun et al. (2025)	20 women with PCOS and obesity	Liraglutide 1.2 mg/day – 12 weeks	17 endometrial gene pathways altered; inflammatory and metabolic modulation; potential improvement in endometrial receptivity.
Su et al. (2025)	207 women with PCOS (135 obese)	Liraglutide up to 1.8 mg/day – 6 months	↓ BMI (~29 → 24.7 kg/m²); ↓ serum/follicular leptin; ↑ LEP promoter methylation in granulosa cells.
Xing et al. (2022)	60 women with PCOS and overweight	Metformin vs Metformin + Liraglutide 1.2 mg/day – 12 weeks	Menstrual regularity 88.0% vs 92.6%; greater ↓ testosterone and ↑ SHBG in the combination group.

In the randomized clinical trial conducted by Elkind-Hirsch et al.,[12] liraglutide monotherapy promoted a mean body weight reduction of 5.7% over 32 weeks, associated with a significant decrease in the free androgen index (FAI) and an increase in menstrual regularity. This study is particularly relevant because it demonstrates that, even in the absence of metformin, isolated metabolic improvement was sufficient to impact indirect reproductive markers, suggesting partial restoration of ovulatory function. The longer follow-up period (32 weeks) may explain the greater effect on menstrual cyclicity when compared with shorter interventions, such as that of Xing et al. (2022), in which 12 weeks may be sufficient for initial changes but not for sustained stabilization of the menstrual cycle.

The systematic review by Bader et al.,[7] aggregating data from 486 women with PCOS, reinforces the robustness of these findings by demonstrating that reductions in body mass index (BMI), waist circumference, and insulin resistance are consistent effects of GLP-1RAs, particularly liraglutide and exenatide. However, the authors highlight that reproductive outcomes were more heterogeneous, with some studies reporting menstrual normalization and/or reductions in total testosterone, while others showed more modest effects. This suggests that reproductive impact depends on the magnitude of metabolic response, PCOS phenotype, and duration of exposure. Such heterogeneity is also evident when comparing monotherapy versus combination therapy, reinforcing that reproductive restoration tends to accompany more pronounced metabolic correction.

In the study by Xing et al. (2022), both metformin monotherapy and the combination of metformin plus liraglutide improved menstrual regularity in the short term; however, only the combination group exhibited broader improvement in the gonadal profile, including significant reductions in total testosterone, increased sex hormone–

binding globulin (SHBG), and elevated progesterone levels. These findings support the hypothesis of pharmacological synergy: metformin reduces hepatic glucose production and improves insulin sensitivity, whereas liraglutide acts on appetite control, body weight, and peripheral insulin sensitivity, thereby potentiating normalization of the hypothalamic–pituitary–ovarian axis. This pattern is consistently observed in subsequent studies, in which combination therapy with GLP-1RAs demonstrates greater endocrine and reproductive effects than monotherapy.

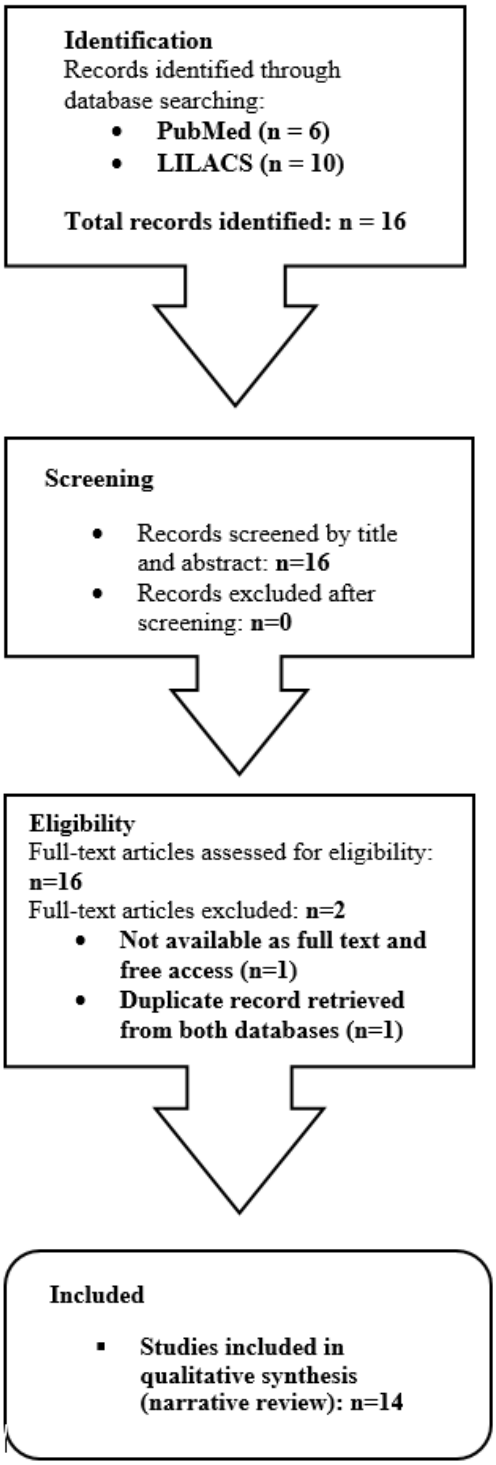

Figure 1 Flowchart of study identification, screening, eligibility, and inclusion adapted from Prisma (2020).

Particularly expressive results were observed by Chen et al.,[13] in which the combination of semaglutide and metformin, compared with metformin alone, resulted in greater weight loss (6.09 kg *vs.* 2.25 kg), superior improvement in menstrual regularity (72.5% *vs.* 42.3%), and increased spontaneous pregnancy after GLP-1RA discontinuation (35% *vs*. 15%). This study is noteworthy for linking metabolic and hormonal effects to a clinically relevant outcome, spontaneous pregnancy, suggesting that therapy may create a "favorable metabolic window" after treatment cessation. This is particularly relevant in preconception care, given that GLP-1RAs should not be used during pregnancy. These findings also help explain discrepancies among studies, as more pronounced metabolic improvement appears to be associated with more evident reproductive outcomes.

The comparison between classical hormonal therapy and metabolic intervention was explored by Liao et al.,[14] who compared cyproterone acetate/ethinylestradiol (CPA/EE) plus metformin *versus* liraglutide plus metformin. While hormonal therapy was superior in directly reducing androgen levels, the GLP-1RA group showed greater weight loss, more pronounced metabolic improvement, and increased ovulation rates. These results reinforce that pharmacological suppression of hyperandrogenism alone, although useful, does not correct the central metabolic determinants of ovulatory dysfunction in PCOS, whereas interventions targeting insulin resistance and central adiposity tend to generate more comprehensive effects on ovulation and menstrual cyclicity.

The case report by Nicolaou et al.,[15] despite its lower level of evidence, contributes to the understanding that exenatide may restore menstrual cyclicity and improve hormonal parameters even before significant weight loss occurs, indicating potential central and neuroendocrine mechanisms beyond weight reduction alone. This observation aligns with the concept that GLP-1RAs may modulate inflammatory pathways and the neuroendocrine axis, contributing to early reproductive responses in specific clinical profiles.

Beyond clinical and hormonal outcomes, the study by Salamun et al.[16] adds a molecular dimension by demonstrating that liraglutide can modify the endometrial transcriptome during the implantation window. In infertile women with PCOS and obesity treated for 12 weeks and achieving ≥5% weight loss, 17 canonical pathways were differentially expressed, involving GLP-1 receptor activation, energy metabolism, inflammatory response, oxidative stress, and intracellular signaling pathways, including PI3K/AKT signaling. This finding is crucial because it expands biological understanding: in addition to favoring ovulation through metabolic improvement, GLP-1RAs may influence endometrial receptivity, a key component of implantation, particularly relevant in women with PCOS who may experience implantation failure even after ovulation is restored.

Accordingly, the meta-analysis by Huang and He,[17] synthesizing randomized clinical trials, demonstrated that liraglutide plus metformin is superior to metformin alone in reducing BMI, improving HOMA-IR, decreasing androgenic markers, and improving menstrual regularity. Although pregnancy was not evaluated as a primary outcome, the observed metabolic–endocrine profile supports the hypothesis of a favorable environment for ovulation. In terms of safety, gastrointestinal adverse events (nausea, vomiting, diarrhea) were more frequent, but without an increase in serious adverse events, reinforcing applicability in the preconception period with appropriate tolerability management.

Furthermore, Su et al.[18] provided robust epigenetic evidence by evaluating 207 women with PCOS (135 obese treated with liraglutide for six months) and demonstrating expressive metabolic and hormonal

improvement, including reductions in BMI (≈29.1 → 24.7 kg/m²), fasting insulin, HOMA-IR, triglycerides, testosterone, and estradiol, alongside increases in HDL, LH, and the LH/FSH ratio. The most innovative finding was the reversal of hypomethylation of the leptin (LEP) gene promoter in granulosa cells following liraglutide treatment, accompanied by reduced serum and follicular leptin levels, suggesting an epigenetic mechanism modulating the ovarian microenvironment. In agreement with Salamun et al.,[16] which reported endometrial modulation, Su et al.[18] reinforces a multifocal action involving both ovarian and endometrial compartments, strengthening the biological plausibility of reproductive effects beyond weight loss.

At the level of meta-analytic evidence focused on exenatide, Hu et al.[19] included nine randomized controlled trials (1,149 women; 12–24 weeks) and demonstrated superiority of exenatide over metformin for pregnancy rate (RR 1.85; 95% CI 1.19–2.86), as well as reductions in total testosterone (SMD −0.43), increases in FSH (MD 0.82), and significant elevations in SHBG (MD 5.00). Metabolically, reductions were observed in HOMA-IR (MD −0.68), fasting insulin (SMD −0.61), body weight (MD −1.69 kg), BMI (MD −1.13 kg/m²), waist circumference (MD −2.49 cm), and waist-to-hip ratio (MD −0.02). Combination therapy with exenatide plus metformin yielded additional benefits, including further increases in SHBG (MD 10.38) and reductions in FAI (MD −3.34), reinforcing the superiority of combination approaches. Regarding safety, a lower incidence of diarrhea was observed compared with metformin (RR 0.11), with no significant differences in other gastrointestinal events. Compared with liraglutide and semaglutide studies, these data suggest a class effect in metabolic and hormonal correction, with a favorable reproductive signal for clinical pregnancy in certain scenarios.

The systematic review and meta-analysis by Peng et al.,[20] including 27 randomized controlled trials and 4,608 infertile women with PCOS, advanced the discussion by evaluating primary outcomes of clinical pregnancy and live birth. For clinical pregnancy, interventions such as pioglitazone alone, clomiphene citrate plus exenatide (CC+EXE), and clomiphene citrate plus metformin plus pioglitazone ranked among the most effective, highlighting the presence of exenatide in higher-probability regimens. However, for live birth, no intervention demonstrated statistically significant superiority over placebo, reinforcing that despite improvements in ovulation and clinical pregnancy, evidence for final reproductive outcomes remains limited. A critical aspect of this study was BMI-stratified analysis: in obese women with PCOS, no intervention, including exenatide, significantly improved clinical pregnancy, contrasting partially with more recent studies such as Chen et al.,[13] in which more intense metabolic improvement was associated with favorable outcomes. This divergence suggests that the magnitude of weight loss and insulin resistance improvement may be decisive for reproductive benefits in obese women, and that less intensive interventions may not surpass the necessary "metabolic threshold."

Additionally, Ling et al.[21] reinforced consolidated evidence that liraglutide plus metformin offers superior metabolic, hormonal, and reproductive benefits compared with metformin alone in women with PCOS and overweight or obesity, with greater reductions in weight and BMI and improvements in glycemic and lipid parameters. Within the endocrine–reproductive axis, the authors reported reductions in androgen levels and improvements in menstrual regularity, ovulation, and spontaneous conception, aligning with the clinical trials by Xing et al. (2022) and the indirect reproductive benefits discussed across studies. In terms of safety, the higher incidence of gastrointestinal events in the liraglutide group, without an increase in serious adverse events, corroborates findings from Elkind-Hirsch et al.,[12] Huang and He,[17] and Hu et al.,[19] consolidating a manageable tolerability profile.

Moreover, Kesavan et al.[23] provided important quantitative evidence by comparing exenatide with metformin and demonstrating superiority of exenatide in reducing BMI (MD 0.51 kg/m²; 95% CI 0.07–0.96) and significantly lowering testosterone levels (MD 0.15; 95% CI 0.07–0.22), with no significant effects on LDL-C or HDL-C. These findings reinforce that lipid improvement may not be the primary reproductive mechanism, whereas reduction of hyperandrogenism and metabolic improvement are more directly linked to ovulation and menstrual regularity. This study aligns with Hu et al.,[19] and clinical trials, reinforcing the consistency of androgen modulation as a central axis for reproductive improvement in PCOS.

Finally, Gill and Mackey[6] provide an essential clinical–pathophysiological framework by integrating adiposity, low-grade inflammation, adipokines, and reproductive axis dysfunction. The authors highlight that adipose tissue functions as an active endocrine organ and that weight loss of ≥5–10% may represent a clinical threshold for improving ovulation and fertility, supporting findings from studies such as Elkind-Hirsch et al.,[12] and aligning with response criteria associated with endometrial changes reported by Salamun et al.,[16] Gill and Mackey[6] also emphasize that GLP-1RAs should be used in the preconception period with adequate planning and contraception during treatment, reinforcing that observed reproductive benefits should be interpreted as indirect effects obtained prior to attempts at conception.[23]

Overall, the 14 studies analyzed support the guiding question of this narrative review by demonstrating that GLP-1 receptor agonists exert a multifactorial impact on female fertility:

(i) Reduction of central adiposity and insulin resistance

(ii) Modulation of hyperandrogenism and reproductive axis markers (SHBG, free androgen index, gonadotropins)

(iii) Improvement of menstrual cyclicity, ovulation, and, in specific contexts, clinical or spontaneous pregnancy

(iv) Emerging evidence of action at the endometrial (transcriptomic) and ovarian (epigenetic) levels.

At the same time, important limitations remain, including methodological heterogeneity, variability in treatment duration, diverse sample sizes, and scarcity of final reproductive outcomes such as live birth and implantation, particularly evident in network meta-analyses. Nevertheless, the body of evidence indicates that GLP-1RAs constitute promising adjuvant therapeutic strategies in the preconception management of women with PCOS and obesity, provided they are used with appropriate reproductive counseling and discontinued prior to conception attempts.

Conclusion

The present narrative review demonstrates that glucagon-like peptide-1 receptor agonists exert relevant, albeit indirect, effects on female fertility, particularly in women with polycystic ovary syndrome associated with obesity and insulin resistance. The analyzed studies indicate that agents such as liraglutide, semaglutide, and exenatide consistently improve metabolic and hormonal profiles, promoting reductions in body weight, insulin resistance, and hyperandrogenism, key factors in the pathophysiology of ovulatory dysfunction.

Beyond systemic effects, emerging evidence suggests potential direct actions of these agents on the reproductive microenvironment,

including endometrial transcriptomic alterations and epigenetic modulation in ovarian granulosa cells, thereby expanding the biological plausibility of their influence on reproductive function. These findings reinforce the understanding that GLP-1 receptor agonists act at multiple levels, integrating metabolic, endocrine, and tissue-specific mechanisms that may favor the restoration of ovulation and menstrual cyclicity, as well as increased rates of clinical pregnancy in selected contexts.

Nevertheless, the available data remain heterogeneous, particularly regarding final reproductive outcomes such as live birth, and are limited by methodological issues related to follow-up duration, variability of study populations, and heterogeneity of study designs. Moreover, given that GLP-1 receptor agonists are contraindicated during pregnancy, their use should be restricted to the preconception period, with appropriate reproductive planning and prior treatment discontinuation.

Therefore, GLP-1 receptor agonists may be considered promising therapeutic tools for metabolic and endocrine preparation in women of reproductive age, especially those with polycystic ovary syndrome; however, they should not be regarded as direct fertility-inducing agents. Further well-designed, long-term randomized clinical trials are needed to better elucidate the effects of GLP-1 receptor agonists on female fertility, clarify their impact on gestational outcomes, and establish more precise clinical recommendations for their safe and effective use in female reproductive health.

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Conflicts of interest

Author declares that there is no conflicts of interest.

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