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Effect of hyperandrogenism in obese PCOS patients: GLP-1 receptor agonists plus metformin versus metformin monotherapy–a systematic review and meta-analysis

Penanganan Hiperandrogenisme pada Pasien PCOS dengan Obesitas: Agonis Reseptor GLP-1 Dikombinasikan dengan Metformin Versus Metformin Monoterapi–Suatu Tinjauan Sistematis dan Meta-analisis

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ABSTRACT

Background: *Polycystic ovary syndrome (PCOS) is a common endocrine disorder in reproductive-aged women, characterized by hyperandrogenism, ovulatory dysfunction, and metabolic disturbances, particularly in overweight and obese individuals. Insulin resistance and excess adiposity worsen androgen excess, emphasizing the need for therapies targeting both metabolic and hormonal imbalance.*
Objective: *To evaluate the effectiveness of GLP-1RA plus metformin compared to metformin alone in reducing hyperandrogenism, measured by sex hormone-binding globulin (SHBG) and free androgen index (FAI), in overweight and obese women with PCOS.*
Methods: *A systematic review and meta-analysis were conducted following PRISMA guidelines. Literature searches were performed in PubMed, Cochrane Library, and ScienceDirect (January 2000–June 2025). Eligible studies included randomized and clinical trials comparing GLP-1RA plus metformin versus metformin alone in overweight/obese women with PCOS, reporting SHBG and/or FAI outcomes. Data extraction, risk of bias assessment (RoB-2), and quantitative synthesis were conducted. Five studies with 252 participants were included.*
Results: *Combination therapy significantly increased SHBG (MD = 7.82; 95% CI: 4.98–10.66; $p < 0.00001$; $I^2 = 31\%$) and reduced FAI (MD = −3.16; 95% CI: −4.09 to −2.23; $p < 0.00001$; $I^2 = 0\%$) compared to metformin alone.*
Conclusion: *GLP-1RA combined with metformin is more effective than metformin monotherapy in improving hyperandrogenism in overweight and obese women with PCOS.*

Keywords: *GLP-1 Agonist, hyperandrogenism, metformin, obese, overweight, PCOS*

ABSTRAK

Latar Belakang: Sindrom ovarium polikistik (PCOS) merupakan gangguan endokrin umum pada wanita usia reproduksi, ditandai dengan hiperandrogenisme, disfungsi ovulasi, dan gangguan metabolik, terutama pada individu dengan kelebihan berat badan atau obesitas. Resistensi insulin dan adipositas berlebih memperburuk kelebihan androgen, sehingga diperlukan terapi yang menargetkan aspek metabolik dan hormonal.
Tujuan: Mengevaluasi efektivitas kombinasi GLP-1RA dan metformin dibandingkan metformin saja dalam menurunkan hiperandrogenisme yang diukur melalui sex hormone-binding globulin (SHBG) dan free androgen index (FAI) pada wanita overweight dan obesitas dengan PCOS.
Metode: Tinjauan sistematis dan meta-analisis dilakukan mengikuti pedoman PRISMA. Pencarian literatur dilakukan di PubMed, Cochrane Library, dan ScienceDirect (Januari 2000–Juni 2025). Studi yang disertakan adalah uji klinis dan randomized yang membandingkan GLP-1RA+metformin dengan metformin saja pada wanita

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overweight/obesitas dengan PCOS serta melaporkan SHBG dan/atau FAI. Ekstraksi data, penilaian risiko bias (RoB-2), dan analisis kuantitatif dilakukan. Sebanyak 5 studi dengan 252 partisipan dianalisis.
Hasil: Terapi kombinasi secara signifikan meningkatkan SHBG (MD = 7,82; 95% CI: 4,98–10,66; p < 0,00001; I^2 = 31%) dan menurunkan FAI (MD = −3,16; 95% CI: −4,09 hingga −2,23; p < 0,00001; I^2 = 0%) dibandingkan metformin saja.
Kesimpulan: Kombinasi GLP-1RA dan metformin lebih efektif dibandingkan monoterapi metformin dalam memperbaiki hiperandrogenisme pada wanita overweight dan obesitas dengan PCOS.

Kata kunci: Agonis GLP-1, hiperandrogenisme, metformin, obesitas, kelebihan berat badan, PCOS

INTRODUCTION

Of the endocrinopathies affecting reproductive-aged women, polycystic ovarian syndrome (PCOS) has the highest prevalence. Within this group, its incidence is thought to be between 6 and 20 percent[1]. Ovulation abnormalities, including oligoand/or anovulation, and hyperandrogenism, characterize the condition. Twenty years ago, in 2003, the Rotterdam criteria were established as the diagnostic criteria for polycystic ovary syndrome[2]. Metabolic issues are of critical clinical importance for PCOS patients, even if these criteria do not cover them. These difficulties may disrupt menstruation, the ovulation process, and hyperandrogenism, which can have negative impacts on health in the long run.

Insulin resistance, poor glucose metabolism, dyslipidemia, hypertension, and metabolic syndrome are prominent symptoms in PCOS patients, who also often have an increased body mass index (BMI) and waist circumference. This variety of concerns is relevant to many PCOS patients, including teenage girls, reproductive-age women, pregnant women, and women who have gone through menopause[3]. Among the most significant metabolic problems experienced by PCOS patients is obesity; in fact, it is estimated that at least half of all PCOS patients are obese[4]. Those with polycystic ovary syndrome (PCOS) are three times as likely to be overweight as those without PCOS.[5] In addition, metabolic syndrome is a complex and multifaceted condition in PCOS patients. During their reproductive years, patients with polycystic ovary syndrome are two to three times more likely to develop metabolic syndrome than healthy individuals[4].

About half to three-quarters of PCOS individuals have insulin resistance (IR)[6]. This malfunction within PCOS is caused by a variety of underlying causes. A problem involving insulin receptors is the most often accepted explanation. When this happens, IR turns into a binding defect due to an imbalance between serine and tyrosine phosphorylation, which is too high[7]. Potentially related processes include microRNA changes seen in polycystic ovary syndrome (PCOS) patients and mitochondrial dysfunction associated with oxidative stress and insulin resistance (IR)[8]. It has also been demonstrated that the pathomechanism of IR involves disruptions in normal gut flora[9].

Approximately 75% of adult women with polycystic ovary syndrome (PCOS) report infertility, and the metabolic and reproductive features of the disease are complicated. Important risk factors for PCOS, including insulin resistance (IR) and hyperacidity, impact these aspects of a woman's health[9]. The exact cause of polycystic ovary syndrome (PCOS) is still unknown, although researchers have identified several potential contributors, including disruptions in the hypothalamic-pituitary-ovarian axis, adrenal dysfunction, genetics, and metabolism[10]. Also, HA is a hallmark of polycystic ovary syndrome. Dapas et al.'s genome-wide association study (GWAS) identified two

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separate PCOS subtypes. One subtype, known as the "reproductive" group, comprised of 21–23% of the participants, had elevated levels of LH and SHBG but low levels of BMI and insulin. The other subtype, known as the "metabolic" group, comprised of 37–39% of the participants, had elevated levels of glucose and insulin but lower levels of SHBG and LH[11].

A sex hormone transporter called sex hormone-binding globulin (SHBG) is produced in the liver. It has a strong affinity for circulating sex steroids and helps control the amount of bioavailable sex hormones in the blood. Consequently, SHBG can be utilized to gauge the extent of hyperandrogenism and determine the effectiveness of therapy[12]. A significant factor in the development of polycystic ovary syndrome (PCOS), serum SHBG may have a bearing on PCOS complications and long-term prognosis. Due to high androgen levels and the presence of compensatory HA and IR, the SHBG concentration in PCOS patients is frequently low[13]. Furthermore, androgens and insulin suppress SHBG production and secretion in the liver. The levels of testosterone in PCOS patients are much higher than in healthy individuals. If blood SHBG levels are low, HA can be a contributing factor[12]. Reduced SHBG levels were associated with obesity-related metabolic abnormalities in PCOS women, according to a meta-analysis[14]. Obesity may impact teenage girls' development and raise PCOS risk, which is concerning given the rising rates of obesity among both children and adolescents. Overweight children are more likely to develop insulin resistance (IR) and polycystic ovary syndrome (PCOS), according to clinical findings.

One possible explanation for the correlation between obesity and polycystic ovary syndrome is that being overweight hinders SHBG production and secretion, which raises testosterone bioavailability. This means that teenage girls are more likely to develop polycystic ovary syndrome if they have relatively low serum SHBG levels[13], [15]. Clinicians may be able to better detect PCOS tendencies and act early to enhance metabolic and reproductive outcomes if they have a better grasp of the function of SHBG in the early development of the condition[16]. First-line treatments for polycystic ovary syndrome (PCOS) include dietary and exercise adjustments; however, these have been shown to have little impact on weight loss or PCOS-related symptoms[17], [18]. The primary usage of medications is in the treatment of other diseases, such as type 2 diabetes (T2DM), hence they have not been publicly authorized for the treatment of polycystic ovary syndrome (PCOS).

Hyperandrogenism in PCOS is worsened by insulin resistance in overweight and obese women, and metformin alone often provides limited benefit, highlighting the need for more effective therapies. GLP-1 receptor agonists show promise through metabolic and potential endocrine effects, and this meta-analysis evaluates their added benefit with metformin in reducing hyperandrogenism to inform more personalized PCOS management.

METHODS

Study design

This research is a scoping review. One of the purposes of conducting a scoping review is to summarize and disseminate research findings in a specific field.

Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) standards were followed in the conduct and reporting of this meta-analysis. A thorough search of the literature was carried out up until June 9th, 2025, using PubMed, ScienceDirect, and the Cochrane Library. Medical Subject Headings (MeSH) is a

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controlled vocabulary developed by the National Library of Medicine and used to index articles in PubMed according to their primary topics.

In this study, MeSH terms were employed to ensure a systematic, consistent, and comprehensive literature search and were combined with free-text keywords to maximize search sensitivity. The specified keywords for the literature search were ("Polycystic Ovary Syndrome"[MeSH] OR "polycystic ovary syndrome" OR PCOS) AND ("Obesity"[MeSH] OR obesity OR overweight OR "body mass index" OR BMI) AND (("Glucagon-Like Peptide 1"[MeSH] OR "glucagon-like peptide-1 receptor agonist" OR "GLP-1 receptor agonist" OR liraglutide OR semaglutide OR exenatide OR dulaglutide OR lixisenatide) AND ("Metformin"[MeSH] OR metformin)) AND ("Randomized Controlled Trial"[Publication Type] OR randomized OR randomised OR "RCT" OR "controlled trial")". This procedure would include articles with pertinent titles and abstracts so they could be thoroughly assessed and put through further qualitative and quantitative examination.

Eligibility criteria

The following inclusion criteria were used to filter the studies: 1) research on the impact of the combination of GLP-1 Agonist and metformin and Metformin alone with measurable results in Overweight/obese patients, and 3) the study's main findings include the mean change in SHBG and FAI. The following exclusion criteria were then established: 1) full-text publications that could not be retrieved; and 2) research designs, interventions, or outcomes that were deemed unsuitable. Figure 1 illustrates the specifics of the research search approach.

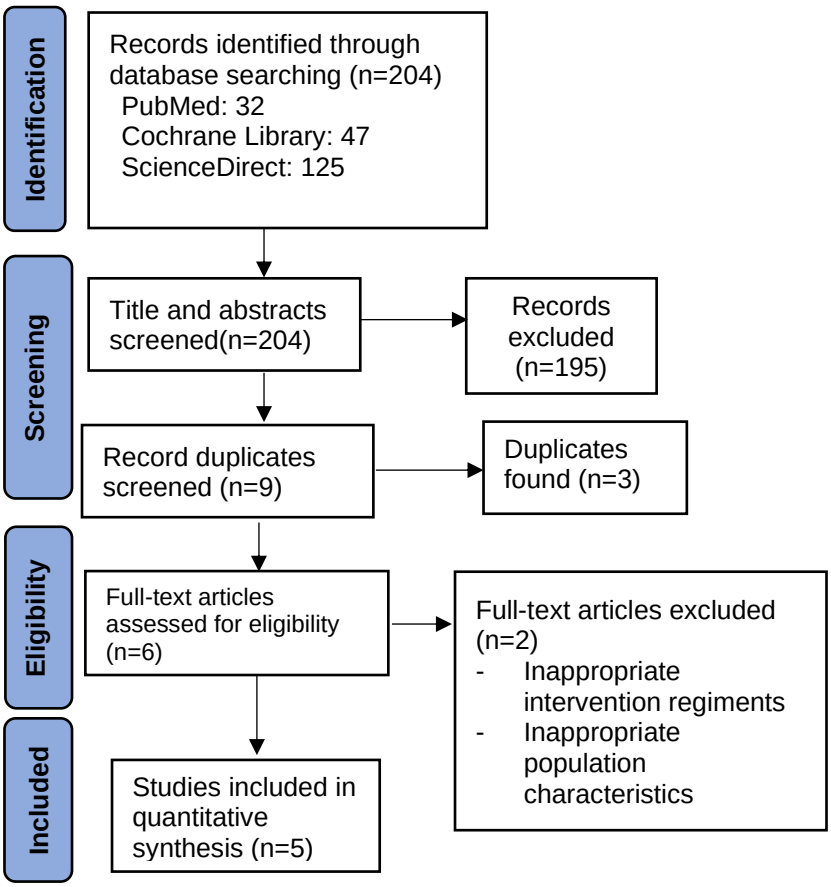

Figure 1. Diagram flow of literature search strategy for this meta-analysis

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Study selection process

Across the included studies, variations existed in the type of GLP-1 receptor agonist, dosage regimens, and duration of therapy. These differences were predefined and extracted as part of the study characteristics. Given the limited number of eligible studies, dose- or duration-based subgroup analyses were not performed. Instead, a random-effects model was applied to account for potential clinical heterogeneity arising from these variations.

Data extraction and risk of bias assessment

Subsequently, we extracted data from our selected articles. Quality assessment was done collaboratively by all reviewers (three reviewers) until consensus was reached. Risk of bias assessment was carried out using RoB-2 tools provided by Cochrane.

Data Analysis

Review Manager version 5.4 (The Nordic Cochrane Centre, Copenhagen) was used for analysis. Effect sizes were expressed as mean differences (MD) with 95% confidence intervals (CI), and pooled using a random-effects model due to expected clinical heterogeneity. Statistical significance was set at $p < 0.05$. Heterogeneity was assessed using the I^2 statistic and categorized as insignificant (0–25%), low (25–50%), moderate (50–75%), or high (>75%). Publication bias was not evaluated due to the limited number of included studies (<10).

RESULTS

A total of 204 records were initially retrieved from PubMed, Cochrane Library, and ScienceDirect (Figure 1). After the removal of duplicates and screening based on titles and abstracts, six articles were assessed in full text. One study was excluded due to an inappropriate intervention, resulting in five studies being included in the final quantitative synthesis. These studies encompassed a combined total of 252 overweight or obese women with PCOS, comparing GLP-1 receptor agonist plus metformin therapy against metformin monotherapy. The primary outcomes evaluated were sex hormone-binding globulin (SHBG) and free androgen index (FAI), both key biochemical indicators of hyperandrogenism. The included trials differed in GLP-1 receptor agonist agents (liraglutide or exenatide), administered doses, and treatment duration, ranging from 12 to 24 weeks. Despite these variations, outcome measures for SHBG and FAI were consistently reported, allowing quantitative synthesis.

All five studies included overweight or obese adult women with PCOS, comparing GLP-1RA (liraglutide or exenatide) plus metformin versus metformin alone over 12–24 weeks. Despite variations in agents and dosages, SHBG and FAI were consistently reported, allowing pooled analysis using a random-effects model. Data were extracted as mean change from baseline with standard deviations, and observed variability likely reflects differences in baseline characteristics and treatment response rather than data inconsistency.

The study by Xing et al. (2022), which enrolled 60 overweight PCOS patients, showed significant improvements in SHBG (11.78 ± 4.95 vs. 5.65 ± 4.32) and FAI (-7.75 ± 1.74 vs. -4.81 ± 3.55) in the combination therapy group compared to metformin alone.[19] Tao et al. (2021) echoed similar findings in a 100-participant RCT, with SHBG increasing more robustly in the combination arm and FAI decreasing more notably than in controls, despite some variability in SHBG standard deviation values. Salamun et al. (2018) reported changes in SHBG with higher variability due to a smaller sample size but reinforced the trend of greater SHBG elevation in the GLP-1RA + metformin group[20].

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Hirsch et al. (2008), using exenatide in 40 obese participants, also found a pronounced difference in both SHBG and FAI, favoring combination therapy[21]. The fifth study, Sever et al. (2014), although smaller in size, demonstrated consistency in directionality with other trials and contributed to the strengthening of the pooled estimate.[22] The meta-analysis for SHBG (five studies, 252 participants) showed a pooled mean difference (MD) of 7.82 (95% CI: 4.98 to 10.66; $p < 0.00001$), with low heterogeneity ($I^2 = 31\%$). This signifies a statistically and clinically significant increase in SHBG levels among those receiving GLP-1RA and metformin compared to metformin alone. The consistency across diverse trials strengthens confidence in the reproducibility of this finding across clinical contexts.

For FAI, data from four studies were pooled, resulting in a mean difference (MD) of -3.16 (95% CI: -4.09 to -2.23; $p < 0.00001$) favoring combination therapy. Notably, heterogeneity was 0%, indicating strong agreement among studies and reinforcing the reliability of this result. The significant decrease in FAI suggests a more effective reduction in free testosterone levels with GLP-1RA combination therapy. Clinically, the observed SHBG elevation and FAI reduction are pivotal, as these markers directly reflect androgen activity and availability. Improved SHBG levels reduce circulating free testosterone, thereby alleviating androgenic symptoms. Decreases in FAI correspond with clinical improvements in menstrual regularity, ovulation, and dermatological manifestations of hyperandrogenism.

Table 1. Characteristics and results of the included studies

Author, year	Study design	Population & Sample	Intervention	Control	Change in SHBG				Change in FAI				Treatment
					Intervention	SD	Control	SD	Intervention	SD	Control	SD	
Xing, 2022	RCT	Overweight (≥24kg/m2) patients with PCOS Intervention: 30 Control: 30	1000mg of metformin p.o + 1.2mg of Liragutide s.c	1000mg of metformin p.o	11.775	4.947	5.65	4.32	-7.75	1.74	-4.81	3.546	12 weeks
Tao, 2021	RCT	Overweight (≥24kg/m2) patients with PCOS Intervention: 50 Control: 50	1500-2000mg of metformin + 10-20ug Exenatide injection	1500-2000mg of metformin	9.12	6.24	3.3	31.93	-2.39	19.47	-2.25	4.359	24 weeks
Salamun, 2018	Pilot study	Obese (≥30 kg/m2) PCOS Patients Intervention: 13 Control:14	1000mg of metformin p.o + 1.2mg of Liragutide s.c	1000mg of metformin p.o	10.8	17.56	4	12.758					12 weeks
Hirsch, 2008	RCT	Obese (≥27kg/m2) patients with PCOS	1500-2000mg of metformin +	1000mg of	11.1	5.243	0.2	5.243	-4.7	2.081	-1.2	2	24 weeks

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Author, year	Study design	Population & Sample	Intervention	Control	Change in SHBG				Change in FAI				Treatment
					Intervention	SD	Control	SD	Intervention	SD	Control	SD	
		Intervention: 20 Control: 20	10ug Exenatide injection	metformin p.o									
Sever, 2014	RCT	Obese (≥30 kg/m2) PCOS Patients Intervention: 11 Control: 14	1000mg of metformin p.o + 1.2mg of Liragutide s.c	1000mg of metformin p.o	7.5	29.53	4	14.933					12 weeks

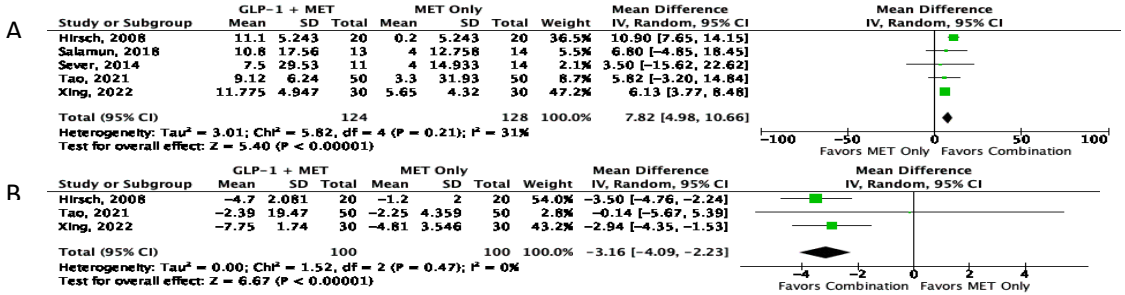

Figure 2. Pooled results for (A) SHGB and (B) FAI between the combination group and metformin monotherapy group

Figure 2 presents the forest plots comparing the effects of GLP-1 receptor agonists plus metformin versus metformin monotherapy on biochemical markers of hyperandrogenism. Panel A shows the pooled mean difference for sex hormone-binding globulin (SHBG), demonstrating a significant increase in SHBG levels favoring the combination therapy. Panel B illustrates the pooled mean difference for free androgen index (FAI), indicating a significant reduction in FAI with GLP-1 receptor agonist combination therapy. A random-effects model was applied, and the direction of effect consistently favored the combination group across included studies. Pooled data indicate that GLP-1RAs plus metformin provide superior biochemical benefits over metformin alone, improving insulin sensitivity, weight, and hormonal imbalance in overweight and obese PCOS patients. These findings suggest a potential endocrine role for GLP-1RAs beyond metabolic effects, though variations in treatment regimens and limited data on long-term outcomes warrant further study.

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DISCUSSION

While biguanide insulin sensitizer metformin (MET) does not influence insulin secretion, it can enhance the effect of insulin. Through its effect, it decreases glucose synthesis in the liver, increases insulin-mediated glucose absorption in skeletal muscle and the liver, and decreases the consumption of gluconeogenic substrates[23]. Metformin has been utilized as an insulin sensitizer for the treatment of polycystic ovary syndrome (PCOS) in obese women since their metabolic features resemble type 2 diabetes mellitus (T2DM) in relation to insulin resistance and hyperinsulinemia[24]. Weight loss, reduced insulin resistance, and reduced testosterone levels are among the metabolic and reproductive effects of MET, according to studies. The compound also restores a regular menstrual cycle and ovulation and regulates ovarian function[25]. Researchers Heidari et al. found that MET may help women with polycystic ovary syndrome (PCOS) by enhancing endothelial function and reducing endothelial dysfunction; however, it had only a moderate impact on glucose metabolism and dyslipidemia[26]. Treatment with MET resulted in notable improvements in sex hormone markers such as T, FSH, and LH in overweight PCOS women, according to Guan et al.; however, MET did not regulate SHBG or androstenedione (A4) to a significant degree[27]. Nausea, vomiting, and gastrointestinal distress are serious adverse effects of MET that may restrict its usage. Worldwide, physicians are seeking innovative treatments for polycystic ovary syndrome (PCOS) due to the documented poor compliance[28].

Both glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) are components of incretin, a hormone released by the intestines that improves the production of insulin in response to glucose[29]. By lowering hepatic glucagon release, decreasing gastric emptying, and suppressing hunger, the incretin hormone helps to regulate weight and enhance glucose metabolism, all of which contribute to glucose homeostasis[30]. The proteolytic enzyme dipeptidyl peptidase-4 (DPP-4) breaks down endogenous GLP-1 more quickly than GIP, which has a half-life of 5 minutes, while its half-life is only 1-2 minutes[31]. Obese and overweight people have reduced incretin secretion and activity, according to most PCOS investigations[32]. The newest example of PCOS treatment, incretin therapy (containing GLP-1RA and DPP-4 inhibitor), is described in the worldwide evidence-based guideline for the evaluation and management of PCOS[18]. By boosting endogenous physiological levels of GLP-1 and GIP, a family of oral anti-diabetic medications known as DPP-4 inhibitors enhances blood sugar management. On the other hand, GLP-1RA replicates the actions of natural GLP-1 to obtain pharmaceutical levels. The DPP-4 enzyme is unable to degrade DPP-4 inhibitors. The metabolic effects of polycystic ovary syndrome (PCOS) can be effectively treated and prevented with the use of GLP-1RA and DPP-4 inhibitors[33], [34].

The pituitary gland secretes less GnRH and has lower GLP-1 mRNA expression than the hypothalamus, although GLP-1 stimulates LH release[35]. Acute intracerebral injection of GLP-1 accelerates the process of ovulation by increasing estrogen, progesterone, and the number of mature follicles. It also causes a rapid rise in LH levels before to ovulation[36]. The ovaries are also sites of GLP-1RA expression; this hormone has the effect of dramatically lowering progesterone levels without changing estrogen production[37]. Women with polycystic ovary syndrome (PCOS) have shown promising weight loss and liver fat reduction results after 26 weeks of therapy with liraglutide, a GLP-1 receptor agonist, as compared to placebo. It may also enhance HA and ovulation, which might lead to changes like higher SHBG levels and lower FT levels. The rise in SHBG levels seen in PCOS women following liraglutide therapy could be attributed to a mix of factors, including weight reduction, improved insulin resistance, and HA

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percent[37], [38]. When compared to MET alone, MET with GLP-1 RAs seems to be more effective in reducing hyperandrogenemia, particularly via raising SHBG, in overweight women with polycystic ovary syndrome (PCOS)[39]. Additionally, Wu et al.'s animal studies demonstrated that compared to the PCOS group caused by DHEA, the groups treated with three different dosages of dulaglutide had much lower blood androgen levels and considerably higher SHBG content[40]. Also, in an animal model of polycystic ovary syndrome (PCOS) brought on by letrozole and a high-fat diet (HFD), we discovered that MET and exenatide can improve glucose and lipid metabolism, reduce hyperandrogenemia, and raise blood SHBG levels. To further understand the function and mechanism of action of incretin-based treatments in elevating SHBG levels and controlling polycystic ovary syndrome (PCOS), larger-scale clinical studies are required, notwithstanding the encouraging therapeutic results of GLP-1RA and DPP-4 inhibitors.

PCOS is an endocrine-metabolic disorder marked by hyperandrogenism, particularly in overweight and obese women, where insulin resistance worsens hormonal imbalance and limits the effectiveness of metformin alone. GLP-1 receptor agonists have emerged as promising adjuncts, and this meta-analysis of five RCTs (n = 252) shows that their combination with metformin significantly improves hyperandrogenism, increasing SHBG (MD 7.82; 95% CI 4.98–10.66) and reducing FAI (MD −3.16; 95% CI −4.09 to −2.23) with low heterogeneity.

These biochemical improvements are clinically significant, as increased SHBG reduces free testosterone and androgenic activity, while decreased FAI reflects lower bioavailable androgens, likely translating into improved symptoms such as hirsutism, acne, and menstrual irregularities. These effects are explained by the complementary actions of metformin and GLP-1RAs, which improve insulin sensitivity, promote weight loss, and restore hormonal balance, with additional potential effects on the hypothalamic-pituitary-ovarian axis, supported by both preclinical and clinical evidence.

Compared to prior systematic reviews that emphasized weight loss and glycemic outcomes, this analysis expands the evidence base by demonstrating that the endocrine benefits of GLP-1RAs are not merely secondary to metabolic changes. The consistent improvement in SHBG and FAI across studies, regardless of specific GLP-1RA agent or study duration, suggests a class effect with genuine endocrine-modulating potential. This reinforces the hypothesis that GLP-1RAs have dual-action benefits in PCOS, targeting both the metabolic and hormonal axes in a coordinated fashion, which is especially advantageous in patients with a severe phenotype marked by obesity and insulin resistance.

This analysis is limited by the small number of studies despite a moderate total sample size (n = 252), limited reporting of clinical outcomes, and variability in GLP-1RA regimens and outcome reporting, which may affect generalizability; residual heterogeneity also cannot be excluded. Nonetheless, GLP-1RA plus metformin appears beneficial for overweight and obese PCOS patients, particularly those with persistent symptoms or insulin resistance, supporting its integration into clinical practice. Further large, multicenter RCTs with longer follow-up and comprehensive outcomes, including fertility, are needed.

CONCLUSION

In conclusion, GLP-1 receptor agonists combined with metformin are superior to metformin alone in improving hyperandrogenism (SHBG and FAI) in overweight and obese women with PCOS, supporting their role as an effective, multifaceted approach targeting both metabolic and hormonal dysfunction.

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