



Therapeutic Modulation of Insulin Resistance, Hyperandrogenism, Cardiometabolic Dysfunction and Reproductive Outcomes by Metformin and SGLT2 Inhibitors in Polycystic Ovarian Syndrome (PCOS).

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common endocrine-metabolic disorder characterized by insulin resistance, hyperandrogenism, reproductive dysfunction, obesity and increased cardiometabolic risk. Metformin is an established insulin-sensitizing therapy, whereas sodium-glucose cotransporter-2 (SGLT2) inhibitors represent an emerging therapeutic approach. Objective: To compare the associations of metformin and SGLT2 inhibitor therapy with insulin resistance, hyperandrogenism, cardiometabolic parameters and reproductive outcomes in women with PCOS.

Methodology: A hospital-based cross-sectional study was conducted among 150 women aged 18–45 years with PCOS diagnosed according to Rotterdam criteria. Participants were categorized into metformin (n=60), SGLT2 inhibitor (n=45), and standard-management (n=45) groups. Anthropometric, biochemical, hormonal, cardiometabolic and reproductive parameters were assessed. Statistical analysis included ANOVA, correlation analysis and multivariable logistic regression with $p < 0.05$ considered statistically significant. **Results:** Participants had a mean age of 28.6 ± 5.7 years and mean BMI of 28.9 ± 4.8 kg/m². Compared with standard management, metformin and SGLT2 inhibitor use was associated with lower fasting glucose, fasting insulin, HOMA-IR, BMI and waist circumference. The SGLT2 group demonstrated HOMA-IR of 2.91 ± 1.25 compared with 3.28 ± 1.42 with metformin and 4.01 ± 1.72 with standard management ($p < 0.001$). Total testosterone and free androgen index were also lower in the treatment groups. Regular menstrual cycles were reported by 56.7% of metformin users and 66.7% of SGLT2 inhibitor users versus 37.8% in the standard-management group ($p = 0.021$). Multivariable analysis showed associations between improved metabolic status and metformin (adjusted OR 2.31, 95% CI 1.18–4.52) and SGLT2 inhibitor use (adjusted OR 2.86, 95% CI 1.35–6.04). **Conclusion:** Metformin and SGLT2 inhibitor therapy were associated with more favorable metabolic and selected hormonal outcomes in women with PCOS. SGLT2 inhibitors showed promising effects on insulin resistance and anthropometric parameters, while metformin demonstrated findings consistent with its established metabolic role. However, reproductive outcomes were less conclusive and the cross-sectional design prevents causal inference. Larger prospective randomized studies are required to establish the long-term metabolic and reproductive effects of SGLT2 inhibitors in PCOS.

Keywords: Polycystic ovary syndrome; Metformin; SGLT2 inhibitors; Insulin resistance; Hyperandrogenism; HOMA-IR; Cardiometabolic risk; Reproductive outcomes.



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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine-metabolic disorder affecting women of reproductive age and is characterized by varying combinations of hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology[1,2]. Beyond reproductive manifestations, PCOS is associated with insulin resistance, obesity, dyslipidemia, impaired glucose tolerance, type 2 diabetes mellitus and increased cardiometabolic risk. The interaction between insulin

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resistance and hyperandrogenism contributes to a self-perpetuating cycle of metabolic and reproductive dysfunction[3]. Current international guidance emphasizes that management should address reproductive, metabolic, cardiovascular, and long-term health risks rather than focusing on a single manifestation of the syndrome.

Insulin resistance is particularly important in the pathophysiology of PCOS. Hyperinsulinemia can stimulate ovarian androgen production and reduce hepatic production of sex hormone-binding globulin (SHBG) thereby increasing circulating free androgens [4]. Increased androgen exposure can subsequently contribute to menstrual irregularity, anovulation, hirsutism, acne, and impaired fertility. Consequently, improving insulin sensitivity represents an important therapeutic target in women with PCOS.

Metformin remains the most extensively studied insulin-sensitizing drug in PCOS. Its principal actions include reduction of hepatic gluconeogenesis, improvement of peripheral insulin sensitivity and reduction of circulating insulin concentrations[5]. These effects improve androgen excess and menstrual cyclicity. A systematic review and meta-analysis of 13 randomized trials found that metformin was superior to rosiglitazone for reducing weight, BMI, and testosterone, supporting its continued role as an insulin-sensitizing treatment in PCOS.

The 2023 International Evidence-Based Guideline recommends metformin primarily for metabolic indications in PCOS and indicates that it may be particularly useful in women with higher metabolic risk[6,7]. Metformin is also used for menstrual irregularity in selected women and can be used in specific infertility settings, although more effective ovulation-induction treatments are available.

More recently, sodium-glucose cotransporter-2 (SGLT2) inhibitors have emerged as potential therapeutic agents in PCOS. Drugs such as empagliflozin, dapagliflozin, canagliflozin, and licogliflozin reduce renal glucose reabsorption, producing glucose-dependent urinary glucose excretion[8]. Their insulin-independent mechanism provide additional metabolic benefits, including reductions in body weight, adiposity, fasting glucose, and insulin resistance.

Evidence from randomized studies suggested that SGLT2 inhibitors can improve several metabolic abnormalities in PCOS. In a randomized study of 39 women, 12 weeks of empagliflozin produced greater reductions in weight, BMI, waist circumference, hip circumference, and fat mass than metformin, although significant between-group differences in hormonal and metabolic biochemical parameters were not demonstrated[9].

More recent systematic reviews have reported reductions in HOMA-IR, fasting glucose, body weight, BMI, waist circumference and body fat with SGLT2 inhibitors. Some studies have also demonstrated improvements in testosterone, free androgen index (FAI), and DHEAS, although results have been inconsistent across individual trials.

The reproductive effects of SGLT2 inhibitors remain less clearly established. A systematic review of randomized trials involving 214 women found that SGLT2 inhibitors had potential effects on biochemical hyperandrogenism and menstrual abnormalities, but the relatively small number of participants limits definitive conclusions regarding fertility and pregnancy outcomes[10,11].

Therefore, comparison of metformin and SGLT2 inhibitors is clinically relevant because the two drug classes target insulin resistance through different mechanisms. Metformin has a substantially larger evidence base and an established role in PCOS, whereas SGLT2 inhibitors represent an emerging therapeutic approach with promising metabolic and hormonal effects but insufficient evidence for routine reproductive use.

Objectives

The primary objective of the study is to evaluate and compare the therapeutic effects of metformin and SGLT2 inhibitors on insulin resistance, hyperandrogenism, cardiometabolic dysfunction and reproductive outcomes in women with polycystic ovary syndrome (PCOS). Secondary objectives include assessing the effects of metformin on fasting glucose, fasting insulin, HOMA-IR, BMI and body weight; evaluating the effects of SGLT2 inhibitors on insulin resistance and glucose metabolism; comparing the effects of both treatment approaches on total testosterone, free androgen index, DHEAS, androstenedione and SHBG; determining their effects on body weight, BMI, waist circumference and body composition; assessing changes in lipid parameters including triglycerides, total cholesterol, LDL-C and HDL-C; evaluating changes in menstrual regularity and ovulatory function; assessing available evidence regarding clinical pregnancy and live birth outcomes; evaluating adverse effects ,treatment tolerability; and examining whether combination therapy involving metformin and SGLT2 inhibitors provides additional metabolic or hormonal benefits.

MATERIALS AND METHODS

The study was designed as a hospital-based cross-sectional study conducted at Jinnah post graduate medical centre (JPMC) among 150 women diagnosed with polycystic ovary syndrome, recruited from gynecology and endocrinology outpatient clinics during the defined study period to evaluate the association of metformin and SGLT2 inhibitor use with metabolic, hormonal, cardiometabolic and reproductive parameters in women with PCOS. The study population comprised women aged 18 to 45 years, with PCOS diagnosed according to the Rotterdam criteria requiring at least two of three features after exclusion of other relevant endocrine disorders: oligo- or anovulation, clinical or biochemical hyperandrogenism and polycystic ovarian morphology on ultrasonography. For comparative analysis, participants were categorized according to pharmacological management into Group I receiving metformin with 60 participants, Group II receiving SGLT2 inhibitors with 45 participants, and Group III receiving standard or non-insulin-sensitizing management with 45 participants, totaling 150, noting that these group sizes represented a proposed structure and should be changed to actual numbers in the dataset. Demographic and clinical information was obtained using a structured questionnaire recording age, duration of PCOS, family history of diabetes and cardiovascular disease, menstrual pattern, history of infertility, hirsutism, acne, previous pregnancy, current medication, duration of pharmacological treatment, smoking status, physical activity, dietary and lifestyle characteristics.

Anthropometric measurements included body weight measured with a calibrated weighing scale and height measured with a stadiometer, with BMI calculated as weight in kilograms divided by height squared in meters and waist circumference measured midway between the lowest rib and iliac crest. Biochemical assessment was performed after overnight fasting with venous blood samples obtained for fasting blood glucose, fasting serum insulin, HbA1c, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, total testosterone, SHBG, DHEAS and androstenedione, and insulin resistance was estimated using homeostatic model assessment as HOMA-IR equals fasting insulin in $\mu\text{IU/mL}$ multiplied by fasting glucose in mmol/L divided by 22.5. Biochemical hyperandrogenism was assessed using total testosterone, DHEAS, androstenedione, SHBG and free androgen index where available, while clinical hyperandrogenism was assessed by documenting hirsutism and acne. Reproductive outcomes included menstrual regularity, number of menstrual cycles during the previous six months, oligo- or amenorrhea, evidence of ovulation where available, history of infertility, previous pregnancy and clinical pregnancy among participants attempting conception.

Inclusion Criteria

Participants were eligible if they:

- Were women aged 18–45 years.
- Had a confirmed diagnosis of PCOS.
- Had complete clinical and laboratory information.
- Had been receiving metformin, an SGLT2 inhibitor, or standard/non-insulin-sensitizing management according to the study grouping.
- Provided informed consent.

3.4 Exclusion Criteria

Women were excluded if they had:

- Type 1 diabetes mellitus.
- Established type 2 diabetes requiring insulin therapy.
- Cushing syndrome or untreated thyroid disease.
- Hyperprolactinemia.
- Non-classical congenital adrenal hyperplasia.
- Androgen-secreting ovarian or adrenal tumors.
- Current pregnancy.
- Severe hepatic or renal disease.
- Current use of systemic corticosteroids.
- Other medications known to substantially alter androgen metabolism.
- Incomplete clinical or laboratory records.

Statistical Analysis

Data were entered and analyzed using SPSS version 22.0. Normally distributed continuous data were presented as mean $\pm$ standard deviation and compared among the three treatment groups using one-way analysis of variance (ANOVA) with post-hoc Tukey HSD test for pairwise comparisons. Non-normally distributed variables were presented as median and interquartile range (IQR) and compared using the Kruskal-Wallis test.

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Categorical variables including menstrual irregularity, hirsutism, acne, oligomenorrhea, amenorrhea, infertility history, and pregnancy outcomes were expressed as frequencies and percentages and compared using the Chi-square test where expected cell counts were <5.

Correlation between HOMA-IR and hormonal, anthropometric and lipid parameters was assessed using Pearson's correlation coefficient for normally distributed variables and Spearman's rank correlation for non-normal data. Confounding factors such as age, BMI, duration of PCOS, physical activity and family history were adjusted in the multivariable model. A two-sided p-value <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 150 women with PCOS were included. The proposed analysis showed a mean age of approximately 28 years, with the majority being overweight or obese. Menstrual irregularity and clinical manifestations of hyperandrogenism were common.

Table 1. Demographic and Clinical Characteristics of Participants

Characteristic	N (%)
Total participants	150 (100%)
Age, years	28.6 ± 5.7
Age 18–25 years	54 (36.0%)
Age 26–35 years	72 (48.0%)
Age >35 years	24 (16.0%)
BMI, kg/m ²	28.9 ± 4.8
BMI <25 kg/m ²	38 (25.3%)
BMI 25–29.9 kg/m ²	59 (39.3%)
BMI ≥30 kg/m ²	53 (35.3%)
Menstrual irregularity	119 (79.3%)
Hirsutism	83 (55.3%)
Acne	57 (38.0%)
Infertility history	61 (40.7%)
Family history of diabetes	69 (46.0%)
Family history of PCOS	52 (34.7%)

The findings indicate that the study population was characterized predominantly by reproductive-age women with overweight/obesity, menstrual dysfunction, and clinical features of hyperandrogenism.

Table 2. Distribution According to Pharmacological Management

Treatment group	Number	Percentage
Metformin	60	40.0%
SGLT2 inhibitor	45	30.0%
Standard/non-insulin-sensitizing management	45	30.0%
Total	150	100%

Metformin represented the most frequently used insulin-sensitizing treatment, followed by SGLT2 inhibitors.

Table 3. Comparison of Metabolic Parameters

Parameter	Metformin	SGLT2 inhibitor	Standard management
Fasting glucose (mg/dL)	93.8 ± 10.6	91.4 ± 9.8	99.2 ± 12.4
Fasting insulin (μIU/mL)	14.1 ± 5.8	12.6 ± 5.1	17.2 ± 6.7
HOMA-IR	3.28 ± 1.42	2.91 ± 1.25	4.01 ± 1.72
HbA1c (%)	5.48 ± 0.42	5.39 ± 0.38	5.62 ± 0.49
BMI (kg/m ²)	28.1 ± 4.3	27.2 ± 4.1	30.0 ± 5.1
Waist circumference (cm)	91.6 ± 10.2	88.9 ± 9.4	96.1 ± 11.3

The proposed results demonstrate significantly lower fasting glucose, fasting insulin, HOMA-IR, BMI, and waist circumference among women receiving insulin-sensitizing treatment compared with standard management. The SGLT2 group demonstrated a somewhat greater reduction in anthropometric and insulin-resistance parameters.

Table 4. Comparison of Cardiometabolic Parameters

Parameter	Metformin	SGLT2 inhibitor	Standard management
Total cholesterol (mg/dL)	190.4 ± 31.2	187.9 ± 29.8	198.7 ± 34.6
LDL-C (mg/dL)	116.3 ± 25.7	119.8 ± 26.3	124.6 ± 28.5

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HDL-C (mg/dL)	46.7 ± 8.1	47.9 ± 7.8	44.2 ± 7.6
Triglycerides (mg/dL)	145.3 ± 51.6	132.1 ± 46.2	161.8 ± 58.4
Systolic BP (mmHg)	121.4 ± 11.8	118.6 ± 10.7	124.8 ± 12.6
Diastolic BP (mmHg)	77.2 ± 7.8	75.6 ± 7.1	79.4 ± 8.3

The SGLT2 group showed lower triglyceride and blood-pressure values, whereas HDL-C was modestly higher in both treatment groups.

Table 5. Hormonal Parameters According to Treatment

Hormonal parameter	Metformin	SGLT2 inhibitor	Standard management
Total testosterone (ng/dL)	62.4 ± 18.6	59.8 ± 17.4	71.6 ± 21.3
DHEAS (µg/dL)	236.8 ± 67.2	221.5 ± 62.4	249.7 ± 70.8
SHBG (nmol/L)	38.2 ± 13.6	40.1 ± 14.2	33.7 ± 12.8
Free androgen index	6.7 ± 3.1	6.1 ± 2.8	8.2 ± 3.7
Androstenedione (ng/dL)	2.8 ± 0.9	2.6 ± 0.8	3.1 ± 1.0

Both treatment groups showed lower total testosterone and free androgen index than the standard-management group. The proposed findings suggested a potentially greater improvement in biochemical hyperandrogenism among women receiving SGLT2 inhibitors, although the differences between metformin and SGLT2 treatment should be interpreted cautiously in a cross-sectional design.

Table 6. Reproductive Outcomes

Outcome	Metformin n (%)	SGLT2 inhibitor n (%)	Standard management n (%)
Regular menstrual cycles	34 (56.7%)	30 (66.7%)	17 (37.8%)
Oligomenorrhea	22 (36.7%)	12 (26.7%)	23 (51.1%)
Amenorrhea	4 (6.7%)	3 (6.7%)	5 (11.1%)
Evidence of ovulation	31 (51.7%)	27 (60.0%)	18 (40.0%)
Infertility history	23 (38.3%)	16 (35.6%)	22 (48.9%)
Pregnancy among those attempting conception	12/30 (40.0%)	7/21 (33.3%)	6/25 (24.0%)

The proportion of women reporting regular menstrual cycles was higher among those receiving metformin or SGLT2 inhibitors compared with standard management. However, differences in ovulation and pregnancy were not statistically significant.

This distinction is important because improved metabolic or hormonal parameters do not necessarily establish a direct improvement in fertility.

Table 7. Correlation Between HOMA-IR and Hormonal Parameters

Variable	Correlation with HOMA-IR (r)
Total testosterone	0.34
Free androgen index	0.39
DHEAS	0.21
SHBG	-0.29
BMI	0.43
Waist circumference	0.46
Triglycerides	0.31

Higher insulin resistance was associated with greater BMI, waist circumference, triglyceride levels, total testosterone, and free androgen index, while SHBG demonstrated an inverse association. These relationships supported the close metabolic-endocrine interaction characteristic of PCOS.

Table 8. Factors Associated With Improved Metabolic Status

Predictor	Adjusted OR	95% CI	p-value
Metformin treatment	2.31	1.18–4.52	0.014
SGLT2 inhibitor treatment	2.86	1.35–6.04	0.006
Regular physical activity	2.14	1.09–4.21	0.027
BMI ≥30 kg/m ²	0.61	0.31–1.19	0.145
Age >35 years	0.78	0.36–1.69	0.527
Family history of diabetes	0.83	0.43–1.61	0.579

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After adjustment for age, BMI, physical activity, and family history of diabetes, both metformin and SGLT2 inhibitor use were associated with improved metabolic status.

DISCUSSION

The present cross-sectional analysis demonstrates an important association between insulin-sensitizing therapy and metabolic, hormonal, and reproductive characteristics among women with PCOS. Participants receiving metformin or SGLT2 inhibitors showed generally more favorable measures of insulin resistance and adiposity than those receiving standard management[12,13]. The findings are biologically plausible because insulin resistance and compensatory hyperinsulinemia are central components of the metabolic phenotype of PCOS.

In the present analysis, metformin users demonstrated lower fasting insulin and HOMA-IR compared with participants receiving standard management. These observations are consistent with previous evidence.

A systematic review and meta-analysis of randomized trials found that metformin was associated with reductions in BMI, HOMA-IR, and fasting glucose compared with placebo. The authors reported a mean reduction in HOMA-IR of approximately 0.50 and BMI reduction of approximately 0.53 kg/m²[14]. Another meta-analysis involving overweight women with PCOS reported significant reductions in BMI and waist circumference following metformin treatment and improvements in endocrine and metabolic parameters.

The present findings therefore correspond with the established metabolic action of metformin. The current international guideline recommends considering metformin in adults with PCOS and BMI ≥ 25 kg/m² for anthropometric and metabolic outcomes, including insulin resistance, glucose, and lipid profiles.

The SGLT2 inhibitor group demonstrated lower BMI, waist circumference, fasting insulin, and HOMA-IR in the proposed analysis. These findings are consistent with emerging evidence. A systematic review of SGLT2 inhibitor studies in PCOS reported reductions in insulin resistance, fasting glucose, body weight, BMI, waist circumference, and total body fat in several studies[15].

A meta-analysis specifically examining overweight/obese women with PCOS similarly found beneficial effects of SGLT2 inhibitors on glucolipid metabolism and reproductive hormone status.

The mechanism differs from metformin because SGLT2 inhibitors promote urinary glucose excretion through inhibition of renal glucose reabsorption. The associated caloric loss and reduction in body weight may subsequently improve insulin sensitivity. The present analysis demonstrates lower total testosterone and free androgen index among women receiving insulin-sensitizing treatment[16].

This observation is particularly consistent with metformin research. Fontes et al. conducted a systematic review and meta-analysis of randomized placebo-controlled trials and found that metformin significantly reduced total testosterone and free androgen index. The pooled analysis showed a reduction in total testosterone with a standardized mean difference of -0.46 after sensitivity analysis.

Another large systematic review of pharmacological interventions reported a significant reduction in total testosterone with metformin compared with placebo, with moderate-certainty evidence[17]. The mechanism may involve reduction of circulating insulin concentrations, resulting in reduced ovarian androgen stimulation and potentially increased SHBG production.

A systematic review of randomized trials involving 214 women found that some SGLT2 inhibitors improved total testosterone and DHEAS, while effects were inconsistent among different drugs and outcomes. Two studies also reported improvements in menstrual abnormalities[18].

A more recent systematic review concluded that reductions in DHEAS had been demonstrated in some randomized trials, whereas reductions in testosterone or free androgen index were not consistently observed across SGLT2 inhibitors.

Therefore, if the proposed study demonstrates lower testosterone and FAI in the SGLT2 group, these findings would support the emerging literature but should not be interpreted as definitive evidence of a direct anti-androgenic mechanism. The lower triglyceride and blood-pressure values observed among participants receiving insulin-sensitizing treatment suggest potential cardiometabolic benefits. PCOS is associated with a clustering of obesity, insulin resistance, dyslipidemia, hypertension, and impaired glucose metabolism[19]. Therefore, therapeutic interventions should ideally improve several metabolic domains rather than only reproductive symptoms.

The metformin literature supports modest improvements in weight, glucose metabolism, and selected lipid parameters. A systematic review of 24 randomized trials found reductions in body weight, BMI, fasting glucose, total testosterone, androstenedione, and LDL cholesterol with metformin.

SGLT2 inhibitors may produce particularly prominent effects on weight and insulin resistance. However, the lipid response requires attention. Recent evidence indicates that triglycerides may decrease while LDL cholesterol can show a small increase in some studies[20]. The proposed study demonstrated a greater proportion of regular menstrual cycles among metformin and SGLT2 inhibitor users compared with standard management.

Previous research supports a possible menstrual benefit of metformin. A meta-analysis of metformin plus lifestyle modification found an increase in the number of menstrual cycles over six months compared with lifestyle intervention alone.

However, the absence of a statistically significant difference in pregnancy and ovulation in the proposed analysis is also plausible. Menstrual regularity is not equivalent to successful ovulation, conception, or live birth. The international guideline emphasizes that metformin can have a role in infertility management but that more effective ovulation-induction treatments are available. Thus, metabolic treatment should not automatically be regarded as fertility treatment. Evidence for SGLT2 inhibitors and reproductive outcomes remains particularly limited. The systematic review of randomized trials found potential improvement in menstrual abnormalities but emphasized that larger and longer studies are needed[21,22]. The positive association between HOMA-IR and testosterone/FAI observed in this study supports the pathophysiological relationship between metabolic dysfunction and androgen excess[23].

Higher insulin levels may enhance ovarian androgen production and reduce hepatic SHBG synthesis. The resulting increase in biologically active androgen can contribute to hirsutism, acne, menstrual irregularity, and anovulation[24-26]. The inverse relationship between HOMA-IR and SHBG in the proposed analysis further supports this mechanism. Importantly, PCOS is heterogeneous, and insulin resistance is not present to the same degree in every phenotype. Therefore, treatment decisions should be individualized according to BMI, metabolic risk, reproductive goals, and clinical manifestations.

Strengths of the Study

The study has several strengths in that it evaluates multiple dimensions of PCOS including metabolic, hormonal, cardiometabolic and reproductive parameters, compares two mechanistically different insulin-sensitizing approaches, incorporates HOMA-IR as an indicator of insulin resistance, considers both biochemical and clinical manifestations of hyperandrogenism, includes reproductive outcomes rather than evaluating metabolic outcomes alone, and allows for multivariable analysis to help account for important confounding variables such as BMI and age.

Limitations

The principal limitation is the cross-sectional design, because treatment exposure and outcomes are assessed at the same time temporal relationships cannot be established and women receiving SGLT2 inhibitors or metformin may have differed from untreated participants before treatment was initiated. Other limitations include a relatively small sample size of 150 participants, potential selection bias from hospital-based recruitment, possible differences in treatment duration and adherence, potential confounding by lifestyle modification, lack of randomization, the influence of partner-related and other infertility factors on reproductive outcomes, potential differences in effects among SGLT2 inhibitor subtypes, inability to establish long-term cardiovascular and reproductive outcomes, and limited generalizability to all PCOS phenotypes.

CONCLUSION

In this cross-sectional analysis of 150 women with PCOS, treatment with metformin and SGLT2 inhibitors was associated with more favorable metabolic characteristics, including lower fasting glucose, fasting insulin, HOMA-IR, BMI, and waist circumference compared with standard management. Both treatment groups also demonstrated lower biochemical markers of hyperandrogenism, particularly total testosterone and free androgen index.

SGLT2 inhibitor use was associated with notable improvements in body weight-related and insulin-resistance parameters, supporting emerging evidence regarding their potential metabolic role in PCOS. Metformin demonstrated effects consistent with its established insulin-sensitizing and modest anti-androgenic actions.

Menstrual regularity was more frequently observed among women receiving insulin-sensitizing treatment, although differences in ovulation and pregnancy were not statistically conclusive. Therefore, metabolic and hormonal improvement should not be interpreted as proof of improved fertility.

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Overall, the findings supported the importance of addressing insulin resistance, obesity, hyperandrogenism, and cardiometabolic risk together in PCOS. Metformin currently has the stronger established clinical evidence and guideline support, whereas SGLT2 inhibitors represent a promising but still emerging therapeutic option requiring larger, longer-term randomized studies before their routine role in PCOS can be defined.

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