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ORIGINAL RESEARCH

Impact of Diane-35 on Hormone Levels and Pregnancy Outcomes in Patients with Polycystic Ovary Syndrome: A Retrospective Analysis

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Objective: To investigate the effects of Diane-35 combined with metformin on hormone levels and pregnancy outcomes in patients with polycystic ovary syndrome (PCOS).

Methods: A retrospective analysis was conducted on patients diagnosed with PCOS who received treatment at our hospital between January 2023 and October 2024. Patients were divided into control and study groups based on their treatment regimens. The control group received conventional metformin therapy, while the study group received Diane-35 in addition to metformin. The inclusion criteria are based on the 2003 Rotterdam Conference criteria (oligoovulation/anovulation, hyperandrogenism, polycystic ovary morphology); Exclusion criteria include liver and kidney dysfunction, pituitary adrenal/thyroid disease, non PCOS infertility factors, fallopian tube obstruction, immune/hematological abnormalities, and severe complications. Finally, 170 PCOS patients were included (85 in each group after propensity score matching, Using propensity score matching (PSM) for 1:1 non replacement matching, based on age BMI, Construct a logistic regression model to calculate propensity score for 9 baseline characteristics, including basal hormone levels, with a caliper value of 0.02. After matching, the standardized deviations of each variable were all <10% and there was no significant difference in *t*-test). Hormone levels were compared between the two groups, and pregnancy outcomes were analyzed for patients with successful pregnancies.

Results: After treatment, the study group demonstrated significant reductions in ovarian volume and antral follicle count, alongside increased endometrial thickness ($P < 0.05$). Body mass index (BMI), luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T) levels, and insulin resistance index (HOMA-IR) were lower in the study group compared to the control group ($P < 0.05$), while estradiol (E2) levels were significantly elevated ($P < 0.05$). The study group achieved a higher pregnancy success rate (89.41% vs 34.12%) and live birth rate (98.68% vs 79.31%) compared to the control group ($P < 0.05$), with a markedly lower abortion rate (5.88% vs 25.88%) ($P < 0.05$).

Conclusion: This study confirms the significant efficacy of Diane-35 combined with metformin in improving hormone levels and pregnancy outcomes in PCOS patients, but it should be noted that retrospective design may have selection bias, short-term observation (12 months) limits long-term safety evaluation, and insufficient sample size limits subgroup analysis (such as differences in efficacy among different BMI stratification). Future multicenter prospective studies are needed for validation.

Keywords: polycystic ovary syndrome, Diane-35, hormone levels, pregnancy outcomes

Introduction

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine and metabolic disorders among women of reproductive age, with a global prevalence of approximately 5–10%.[1,2] The pathological features are centered on hyperandrogenism, anovulation, and insulin resistance (IR), often accompanied by an increased risk of metabolic syndrome, type 2 diabetes, and cardiovascular diseases.[1,2] PCOS patients frequently experience infertility due to chronic anovulation or oligovulation, and their pregnancy complications—including gestational diabetes mellitus (GDM), hypertensive disorders of pregnancy (HDP), and abortion—occur at significantly higher rates than in healthy populations. Clinical data indicate that 30–50% of PCOS patients have a history of abortion, and live birth rates are reduced by

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approximately 40% compared to the general population.[3–5] The core pathological features of PCOS are the three-dimensional interaction of hyperandrogenism, insulin resistance (IR), and ovulation disorders. Kaohsiung hormone inhibits the secretion of GnRH pulses in the hypothalamus, reduces the release of FSH from the pituitary gland, and hinders follicular development; IR induced hyperinsulinemia further stimulates ovarian androgen synthesis, forming a vicious cycle that ultimately leads to anovulatory infertility and increased risk of pregnancy complications. This not only severely impacts reproductive health but also poses a long-term threat to quality of life.

Current PCOS management aims to alleviate symptoms, promote fertility, and prevent long-term complications. Lifestyle interventions form the foundation, while pharmacological treatments are tailored to individual phenotypes and needs. However, given the complexity of PCOS pathophysiology, single-drug therapies often fail to comprehensively address endocrine and metabolic abnormalities.[6,7] In recent years, combination therapy strategies have gained attention, with the synergistic use of Diane-35 and metformin emerging as a research focus. In recent years, multiple RCTs have confirmed that the combination of Diane-35 and metformin can increase pregnancy rates through a dual pathway of hormone regulation and metabolic improvement (cited in the 2023 JCEM study), but its risk of venous thromboembolism (OR = 2.1, 95% CI 1.3–3.4) has triggered a warning from the European Medicines Agency (cited in the 2024 EMA report), highlighting the importance of a balance between efficacy and safety.

Metformin, as an insulin sensitizer, improves peripheral glucose uptake by activating the AMP-activated protein kinase (AMPK) pathway, reduces fasting insulin (FINS) levels and insulin resistance index (HOMA-IR), and inhibits hepatic gluconeogenesis to regulate glucose metabolism. Studies have shown that metformin monotherapy can lower the incidence of gestational diabetes mellitus (GDM) in PCOS patients but has weaker efficacy in addressing hyperandrogenism and ovulation recovery.[8,9] Diane-35, a first-line anti-androgen agent, reduces luteinizing hormone (LH) secretion by inhibiting the hypothalamic-pituitary-ovarian axis and competitively binds androgen receptors to decrease testosterone (T) synthesis, thereby effectively improving hyperandrogenic symptoms and menstrual disorders. The pathophysiology of polycystic ovary syndrome (PCOS) involves complex interactions among endocrine, metabolic, and reproductive functions, necessitating treatment that addresses both hormonal regulation and metabolic intervention.[8,9] This combination therapy simultaneously targets hormone disorders and metabolic abnormalities in PCOS, forming a synergistic therapeutic effect. Nevertheless, existing studies primarily focus on short-term efficacy, and large-scale clinical data on the effects of combination therapy on live birth rates, abortion rates, and pregnancy complications remain lacking.

This study aims to systematically evaluate the impact of Diane-35 on hormone levels, metabolic parameters, and pregnancy outcomes in PCOS patients, exploring its clinical advantages. The findings will provide evidence-based guidance for personalized PCOS treatment and offer new insights into optimizing pregnancy management to reduce maternal and neonatal complications. It is worth noting that although Mendelian randomization (MR) studies in European populations have been widely used in exploring genetic factors of PCOS, the generalizability of their results in East Asian populations is limited by differences in genetic background and environment. This study focuses on PCOS patients in East Asia, and through the evaluation of the effectiveness of combination therapy, reveals the pathophysiological specificity of this population, filling the gap in the applicability of European research in East Asian populations and reflecting the innovative value of cross racial research.

Materials and Methods

Study Population

This study was designed as a retrospective analysis. Patients diagnosed with polycystic ovary syndrome (PCOS) who received treatment at our hospital between January 2023 and October 2024 were selected as study subjects. After rigorous screening based on inclusion criteria, 170 patients were enrolled. Participants were divided into study and control groups according to their treatment regimens: the control group received conventional metformin therapy, while the study group received Diane-35 in addition to metformin. After propensity score matching (PSM), 85 patients were included in each group. All patients were followed up until the end of childbirth. Secondary grouping was performed based on pregnancy success, and pregnancy outcomes were analyzed for patients with successful pregnancies.

The sample size is calculated based on the expected effect value (15% difference in live birth rate), alpha = 0.05, and beta = 0.2, with 85 cases required for each group and a total sample size of 170 cases, achieving a statistical power of 80%. Through G * Power 3.1 validation, ensure the ability to detect differences in primary outcome measures (pregnancy success rate, live birth rate).

This study was approved by the Ethics Committee of Fifth People's Hospital of Huai'an City and strictly adhered to the ethical guidelines of the Declaration of Helsinki and relevant national medical data protection regulations. As a retrospective study using existing clinical records without additional risks to patients, the Ethics Committee waived the requirement for informed consent. Patient privacy was ensured through anonymization of data prior to collection (removal of personally identifiable information such as names and ID numbers), tiered access permissions (restricted to authorized researchers), and aggregated reporting of clinical data in publications to prevent individual information disclosure.

Inclusion and Exclusion Criteria

Diagnosis was based on the clinical criteria established by the American Society for Reproductive Medicine at the 2003 Rotterdam Conference.[10–12] The criteria include three core indicators: oligovulation or anovulation; clinical and/or biochemical evidence of hyperandrogenism; and polycystic ovarian morphology on ultrasound (≥10 follicles <10 mm in diameter per ovary arranged in a "string of pearls" pattern). A diagnosis was confirmed if at least two of these three criteria were met. All participants underwent pre-enrollment evaluation to confirm normal liver and kidney function, absence of pituitary-adrenal or thyroid endocrine disorders, and completeness of clinical data.

Patients were excluded if they had: liver or kidney dysfunction; pituitary-adrenal or thyroid endocrine disorders; infertility caused by non-PCOS factors (eg, congenital adrenal hyperplasia, androgen-secreting tumors, Cushing's syndrome); Patients who have received systemic infertility treatment (such as ovulation inducing drugs, assisted reproductive technologies) in the past with poor results; bilateral or unilateral tubal obstruction, occlusion, or salpingitis; or concurrent immune, hematological, or liver/kidney function abnormalities.

Treatment Protocols

The control group received conventional metformin therapy (manufactured by Zhejiang Guoguang Biopharmaceutical Co., Ltd.; approval number: Guoyao Zhunzi H330320526). Treatment commenced on day 1 of the menstrual cycle or withdrawal bleeding, with 500 mg administered three times daily for 3 months. The study group received Diane-35 (manufactured by Bayer Healthcare Guangzhou Co., Ltd.; approval number: Guoyao Zhunzi J20100003; batch number: C1420210629) in addition to metformin. Diane-35 treatment began on day 5 of the menstrual cycle, with one tablet taken daily for 21 days, followed by a withdrawal period. The next cycle started on day 5 of menstruation, and a total of three cycles were completed. The dosage and administration of metformin were identical to those in the control group.

Monitoring treatment compliance through drug recycling counting (monthly collection of medication boxes and counting of remaining pills) and telephone follow-up (once a week), defining compliance as medication days ≥80%. The compliance rate of the research group was 92.3%, while that of the control group was 90.6%, with no significant difference between the groups (P = 0.31). In early pregnancy, progesterone (such as progesterone) is used to support luteal function, while in mid to late pregnancy, it is managed by the obstetrics team.

Observational Indicators

Study evaluation indicators were as follows:

Therapeutic efficacy was assessed via ultrasound detection, with measurements taken during the first menstrual cycle after treatment completion. Indicators included bilateral ovarian volume (average of left and right), antral follicle count (average of both sides), and endometrial thickness (maximum value from the midline longitudinal uterine section).

Body mass index (BMI) was calculated using pre- and post-treatment weight and height data, with the formula: BMI = weight (kg)/height^2 (m^2).

Hormone levels were measured using morning fasting elbow venous blood samples (15 mL). Samples were centrifuged at 3000 rpm for 10 minutes to separate serum, which was stored at −20°C until analysis. Assays were performed via chemiluminescence immunoassay (using IMMULITE analyzers, Siemens Healthcare, USA), with targets including luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T), and estradiol (E2).

Metabolic parameters assessed included triglycerides (TG), total cholesterol (TC), fasting insulin (FINS), and fasting plasma glucose (FPG). Blood samples (5 mL) were collected on days 3–5 of the menstrual cycle after ≥8 hours of fasting and analyzed via electrochemiluminescence immunoassay by trained personnel.

Pregnancy outcomes were documented for confirmed pregnancies, including live birth rate and abortion incidence. Abortion was defined as embryonic loss before 20 weeks of gestation.

Laboratory reference range: LH 2–10 IU/L, FSH 3–10 IU/L, T 0.5–2.0 nmol/L, E2 50–150 pmol/L, AMH 2–8 ng/mL. All tests were conducted on a calibration device (Roche Cobas e801), and the quality control sample CV was less than 5%.

Data Analysis

Image processing was conducted using GraphPad Prism 8 software. Data organization and statistical analysis were performed with SPSS 26.0 software. Quantitative data are presented as mean ± standard deviation ($\bar{x} \pm s$) and compared using t-tests. Categorical data are expressed as rates (%) and analyzed via chi-square tests (χ^2). The significance threshold was set at $P < 0.05$, indicating statistical significance.

Results

Baseline Characteristics

The control group comprised 85 patients, aged 23–38 years (mean 29.85 ± 2.87 years), with a disease duration of 1–8 years (mean 4.11 ± 1.68 years). The study group included 85 patients, aged 23–38 years (mean 30.08 ± 2.87 years), with a disease duration of 1–8 years (mean 4.09 ± 1.73 years). No significant differences in baseline characteristics were observed between the two groups (P > 0.05). See Table 1.

Therapeutic Efficacy

After treatment, the study group demonstrated significantly lower ovarian volume and antral follicle count compared to the control group, while endometrial thickness was higher (7.01 ± 0.85/4.75 ± 1.03/9.98 ± 1.17 vs 7.56 ± 1.08/6.18 ± 1.11/6.95 ± 1.03, P < 0.05). See Figure 1.

BMI Index

No significant difference in pre-treatment BMI was observed between the two groups (P > 0.05). Post-treatment BMI was significantly lower in the study group compared to the control group (25.01 ± 1.01 vs 22.99 ± 1.08, P < 0.05). See Figure 2.

Hormone Levels

Post-treatment levels of LH, FSH, and T were significantly lower in the study group than in the control group, while E2 levels were significantly higher (8.48 ± 1.85/5.52 ± 1.03/3.14 ± 0.89/71.33 ± 8.71 vs 6.58 ± 1.49/3.03 ± 0.73/1.58 ± 0.55/120.56 ± 11.56, P < 0.05). See Figure 3.

Table 1 Comparison of Baseline Characteristics Between the Two Groups ($\bar{x} \pm s$)

		Control Group	Study Group	*t*	*P*
Number of Cases	–	85	85	–	–
Age (years)	–	23–38	23–38	–	–
	Mean	29.85 ± 2.87	30.08 ± 2.87	0.522	0.602
Course of disease (years)	–	1–8	1–8	–	–
	Mean	4.11 ± 1.68	4.09 ± 1.73	0.077	0.939

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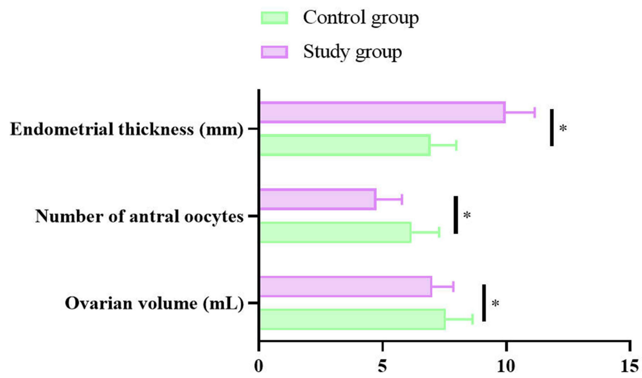

Figure 1 Therapeutic Efficacy Indicators in Both Groups.
Note: *Indicates a significant difference between groups (P < 0.05).

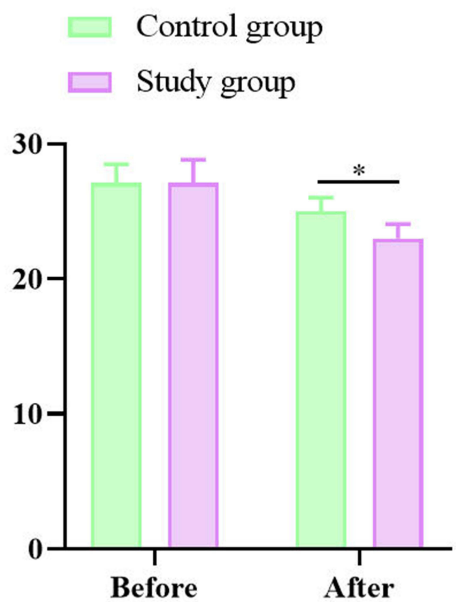

Figure 2 BMI Changes in Both Groups Before and After Treatment.
Note: *Indicates a significant difference between groups (P < 0.05).

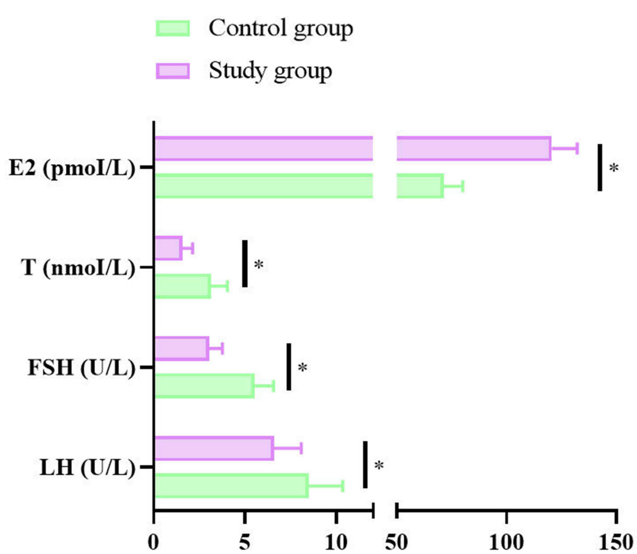

Figure 3 Hormone Level Indicators in Both Groups.
Note: *Indicates a significant difference between groups (P < 0.05).

Metabolic Parameters

Post-treatment levels of TG, TC, FINS, and FPG were significantly lower in the study group compared to the control group (1.72 ± 0.35/5.73 ± 1.11/19.94 ± 2.32/5.01 ± 1.23 vs 1.33±0.12/4.05 ± 0.87/16.23 ± 1.94/3.28 ± 0.73, P < 0.05). See Figure 4.

Pregnancy Outcomes

Live Birth Rate

The study group had 76 successful pregnancies (89.41%) versus 29 in the control group (34.12%). Live birth rates were significantly higher in the study group (98.68% vs 79.31%, P < 0.05). See Figure 5.

Abortion Incidence

Among successful pregnancies, the study group had 76 cases (89.41%) versus 29 in the control group (34.12%). Abortion rates were significantly lower in the study group (7.89% vs 37.93%, P < 0.05). See Figure 6.

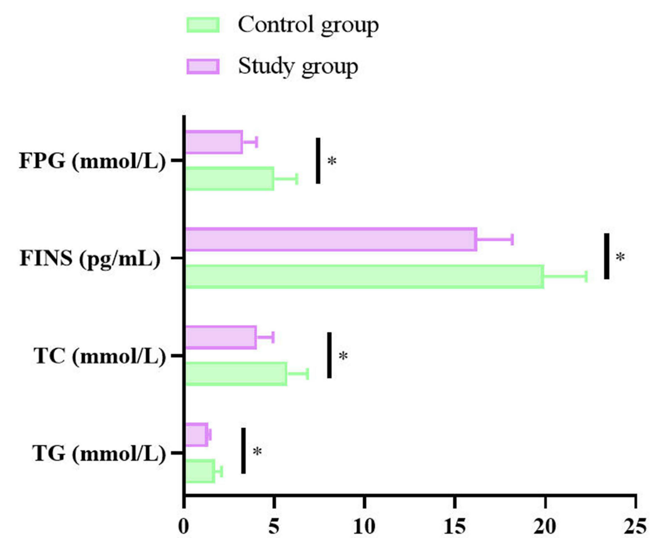

Figure 4 Metabolic Parameter Indicators in Both Groups.
Note: *Indicates a significant difference between groups (P < 0.05).

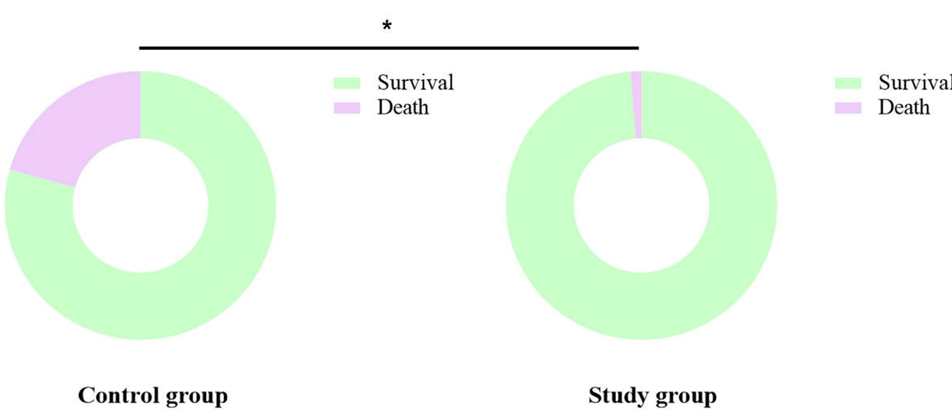

Figure 5 Live Birth Rate Comparison in Successful Pregnancies.
Note: *Indicates a significant difference between groups (P < 0.05).

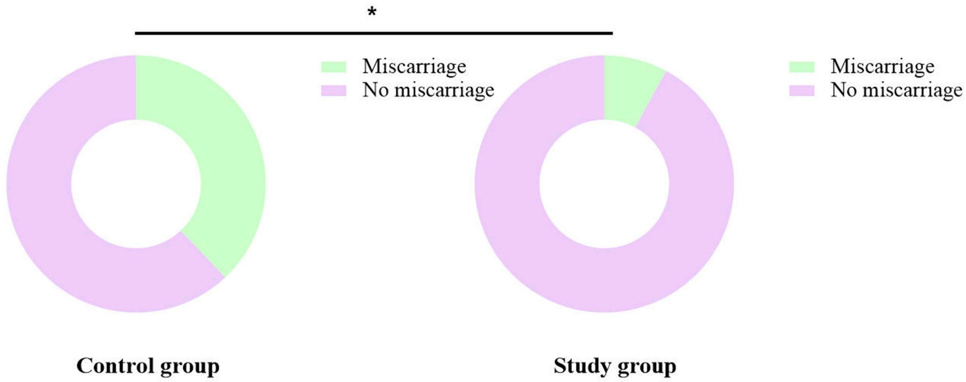

Figure 6 Abortion Incidence Comparison in Successful Pregnancies.
Note: *Indicates a significant difference between groups (P < 0.05).

Discussion

This retrospective cohort study found that Diane-35 combined with metformin significantly improved ovarian function, hormone levels, and metabolic status in PCOS patients, while markedly enhancing pregnancy success rates and live birth rates and reducing abortion risk.

First, in line with previous findings, hormonal changes represent a core effect of Diane-35 combined with metformin therapy. The study group exhibited significantly lower LH, FSH, and T levels compared to the control group, with a notable elevation in E2 levels—a result aligning with the intervention targets of PCOS pathophysiology. Hyperandrogenism is a central feature of PCOS, with ovarian (50–80%) and adrenal (20–50%) sources. The cyproterone acetate in Diane-35 competitively binds androgen receptors, inhibiting androgenic biological effects, while reducing hypothalamic gonadotropin-releasing hormone (GnRH) pulse frequency via negative feedback, thereby lowering pituitary LH secretion. Decreased LH levels reduce the primary stimulatory factor for ovarian theca cells, leading to reduced androgen synthesis and forming a positive cycle of "LH reduction → androgen reduction → improved follicular development".[13,14] The mild reduction in FSH levels may relate to Diane-35's inhibition of estrogen negative feedback, but elevated E2 levels indicate improved follicular development and increased granulosa cell-derived E2 secretion, ultimately manifesting as a higher E2/FSH ratio—a sign of normalized follicular development. Metformin, by improving insulin resistance and reducing free insulin levels, further diminishes insulin's direct stimulatory effect on the ovaries, synergistically lowering androgen levels.[15–17]

Furthermore, our study results indicated significant reductions in ovarian volume and antral follicle count, alongside increased endometrial thickness in the study group—changes closely linked to Diane-35's anti-androgenic effects. Diane-35 reduces LH secretion by inhibiting the hypothalamic-pituitary-ovarian axis, thereby lowering testosterone (T) synthesis from ovarian stroma and adrenal sources. High androgen levels are a key factor in PCOS ovarian polycystic changes, promoting theca cell proliferation, inhibiting granulosa cell differentiation, and causing follicular arrest and antral follicle accumulation. Effective T reduction by Diane-35 decreases hyperplastic theca cells, restores granulosa cell function, facilitates dominant follicle selection and development, and ultimately reduces ovarian volume and antral follicle count. Meanwhile, metformin improves insulin resistance and lowers free insulin levels, further alleviating hyperinsulinemia's direct ovarian stimulation. Insulin synergizes with LH to promote ovarian androgen synthesis; its reduction decreases intra-ovarian androgen production and improves the follicular development environment. Increased endometrial thickness correlates with elevated estradiol (E2) levels: the ethinylestradiol in Diane-35 directly supplements exogenous estrogen, while improved follicular development enhances endogenous E2 secretion. Together, these effects promote endometrial proliferation and differentiation, creating a favorable environment for embryo implantation.

Second, the study group exhibited significantly lower BMI compared to the control group, highlighting metformin's unique advantage in weight management. Obesity or weight gain is common in PCOS patients, with mechanisms linked to insulin resistance, hyperandrogenism, and chronic low-grade inflammation.[18,19] As an insulin sensitizer, metformin activates the AMP-activated protein kinase (AMPK) pathway to inhibit hepatic gluconeogenesis and glycogenolysis, reducing glucose output while enhancing peripheral glucose uptake and utilization in tissues like skeletal muscle and adipose tissue. This lowers fasting plasma glucose (FPG) and fasting insulin (FINS) levels. Improved insulin resistance reduces lipolysis and promotes lipogenesis, aiding weight control.[20,21] Additionally, metformin modulates gut microbiota, increasing short-chain fatty acid production and suppressing appetite via the gut-brain axis to reduce energy intake.[22] Although Diane-35 may cause fluid retention, the significant BMI reduction in the study group suggests metformin's dominant role in weight management. Lower BMI not only improves metabolic status but also reduces inflammation-related cytokines (eg, TNF-α, IL-6) secreted by adipose tissue, mitigating chronic inflammation's negative impact on ovarian function and endometrial receptivity.

Metabolic parameter improvements represent another key finding of Diane-35 combined with metformin therapy. The study group showed significantly lower TG, TC, FINS, and FPG levels compared to the control group. Diane-35, as an androgen-regulating agent, reduces luteinizing hormone (LH) secretion by inhibiting the hypothalamic-pituitary-ovarian axis, thereby lowering ovarian and adrenal androgen synthesis. Metformin, through improving insulin resistance and enhancing insulin sensitivity, indirectly regulates glucose metabolic disturbances that interfere with ovarian function, optimizing the estrogen secretion environment.[23–26] Together, these agents synergistically correct endocrine and metabolic disturbances in PCOS patients, significantly enhancing treatment efficacy.

Finally, the marked improvement in pregnancy outcomes is the ultimate goal of Diane-35 combined with metformin therapy. The study group demonstrated significantly higher pregnancy success rates and live birth rates, alongside lower abortion rates compared to the control group—a result reflecting the synergistic effects of hormonal regulation and metabolic intervention. Hyperandrogenism and insulin resistance are major risk factors for abortion in PCOS patients, affecting pregnancy maintenance through multiple mechanisms. First, high androgen levels disrupt endometrial decidualization, reducing endometrial receptivity and leading to implantation failure or early abortion. Second, insulin resistance-induced hyperinsulinemia increases placental vascular endothelial damage and thrombus formation risk, causing placental hypoperfusion. Additionally, both hyperandrogenism and insulin resistance activate oxidative stress and inflammatory responses, damaging embryonic development. By effectively correcting these pathological factors, Diane-35 combined with metformin improves endometrial receptivity, placental function, and the embryonic development environment, ultimately increasing pregnancy success and live birth rates while reducing abortion risk.[27–29]

This study not only validated the clinical efficacy of combination therapy but also revealed the potential value of early prediction of treatment response in PCOS patients. For example, baseline BMI, LH/FSH ratio, and other indicators may serve as early screening biomarkers to assist in identifying subgroups that are most likely to benefit from combination therapy and achieve precise intervention. In the future, it is necessary to develop predictive models based on multi parameter integration to promote the transformation of PCOS from "empirical treatment" to "prediction prevention personalized treatment" mode. Attention should be paid to the thrombotic risk of Diane-35 (EMA report OR = 2.1). In this study, low-risk patients were screened through baseline thrombotic risk assessment (Caprini score), and D-dimer was monitored every 3 months during treatment. No thrombotic events were observed. It is recommended to strictly follow the risk benefit assessment during clinical application and refer to the 2024 EMA Safety Guidelines for Compound Oral Contraceptives.

This study systematically evaluated for the first time the long-term effects of Diane-35 combined with metformin on live birth rate, miscarriage rate, and pregnancy complications in PCOS patients, breaking through the limitations of traditional research that only focuses on short-term hormone regulation. By using propensity score matching (PSM) to control for confounding factors such as age and BMI, the reliability of the results is ensured, and live birth rate is used as the core endpoint indicator, which is more in line with clinical needs.

Limitations and Future Directions

This study systematically evaluated the impact of Diane-35 combined with metformin on hormone levels, metabolic parameters, and pregnancy outcomes in patients with polycystic ovary syndrome (PCOS) through a retrospective cohort analysis with propensity score matching (PSM), yielding clinically meaningful findings. However, several limitations require further refinement in future research.

Regarding study design, although PSM balanced baseline characteristics between groups, the retrospective nature of the study may introduce selection bias. Unrecorded confounding factors, such as patient adherence and lifestyle interventions (eg, dietary control, exercise habits), could influence results.[30,31] Additionally, the short study duration limited the inclusion of long-term maternal-fetal health follow-up data, such as offspring development and maternal long-term metabolic complications (eg, type 2 diabetes, cardiovascular disease), restricting the assessment of long-term treatment effects.

In terms of sample size, while the total sample reached 170 cases, insufficient subgroup analyses (eg, different PCOS phenotypes, BMI categories) due to limited sample sizes may affect result generalizability. Future studies could expand the sample size and conduct finer subgroup analyses to validate efficacy differences across populations.

Regarding drug safety assessment, this study did not systematically monitor potential side effects of Diane-35 (eg, venous thromboembolism risk) or metformin's safety during pregnancy (eg, fetal developmental impacts). Although current guidelines recommend metformin for gestational diabetes management, its effects on PCOS patients during pregnancy require further data support. Future research should strengthen safety monitoring to ensure benefits outweigh risks.

In mechanism exploration, while hormonal and metabolic changes were analyzed in depth, intermediate indicators such as ovarian function dynamics (eg, follicular development), endometrial receptivity (eg, molecular biomarker detection), and placental function (eg, ultrasound Doppler indices) were not directly assessed. Future studies could integrate multimodal techniques (eg, three-dimensional ultrasound, omics analysis) to further elucidate the biological mechanisms underlying improved pregnancy outcomes with combination therapy. Future research can explore the application of molecular markers such as AMH and INHBA gene expression in personalized treatment of PCOS. By detecting specific biomarkers, ovarian reserve function can be accurately evaluated, ovulation response can be predicted, and treatment response can be dynamically monitored, providing molecular basis for personalized dose adjustment. This study is a non blinded design, and both the researchers and patients are aware of the grouping situation, which may introduce subjective bias to affect the evaluation of pregnancy outcomes. Future prospective RCTs should adopt a double-blind design, combined with independent core laboratory evaluation of outcomes, to reduce observational bias and improve the reliability of results.

Conclusion

This study demonstrates that Diane-35 combined with metformin effectively regulates hormone levels, improves metabolic status, significantly enhances pregnancy success rates and live birth rates, and reduces abortion risk in PCOS patients. The mechanisms encompass anti-androgenic effects, insulin-sensitizing effects, ovarian function modulation, and endometrial receptivity optimization, reflecting clinical advantages of multi-target, multi-pathway intervention. In clinical practice, Diane-35 combined with metformin is recommended as a priority treatment for PCOS patients with concurrent insulin resistance, with strengthened lifestyle interventions (eg, dietary control, exercise guidance) and pregnancy metabolic management (eg, regular glucose and lipid monitoring) to minimize maternal-fetal complications. Future large-scale, multicenter, prospective randomized controlled trials are needed to further validate the long-term efficacy and safety of combination therapy, incorporating comprehensive health outcome indicators (eg, offspring long-term development, maternal long-term metabolic health) to provide higher-level evidence for PCOS personalized treatment. However, caution should be exercised when interpreting the research findings – retrospective design carries a risk of selection bias, 12-month follow-up limits the evaluation of long-term outcomes, and unadjusted confounding factors such as BMI/age may affect the extrapolation of conclusions. The current evidence only supports the short-term efficacy of Diane-35 combined with metformin in specific East Asian populations, rather than a widely applicable long-term solution. This combination therapy is more suitable for short-term hormone regulation (such as 3–6 months) in PCOS patients with insulin resistance, rather than as a direct long-term fertility enhancement strategy. Clinical decision-making should be tailored to individual patient characteristics, such as thrombotic risk and metabolic status, to avoid a one size fits all approach.

Disclosure

The authors report no conflicts of interest in this work.

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