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Comparative Effectiveness of Monotherapy versus Dual Drug Therapy in Glycemic, Lipid, and Renal Outcomes among Women with PCOS-Associated Type 2 Diabetes Mellitus: A Prospective Observational Study

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Abstract

Background

Polycystic ovary syndrome (PCOS) is strongly associated with insulin resistance and metabolic disturbances, increasing the risk of Type 2 Diabetes Mellitus (T2DM). Although oral antidiabetic monotherapy is frequently used as initial treatment, many women fail to achieve adequate metabolic control and require combination therapy.

Methods

This prospective observational study will be conducted at K.M. Medical College Hospital and Research Centre after Institutional Ethics Committee approval. A total of 298 women aged 15–45 years diagnosed with PCOS-associated T2DM will be included and categorized based on prescribed oral hypoglycemic therapy into monotherapy groups (Metformin/Glimepiride) and dual therapy groups (Metformin + Glimepiride). Baseline clinical evaluation and biochemical investigations including fasting blood glucose (FBG), postprandial blood glucose (PPBG), HbA1c, lipid profile, and renal function tests will be performed. Follow-up assessments will be done at 3 months and 6 months. Statistical analysis will be carried out using SPSS software with paired and unpaired t-tests, and p-value <0.05 will be considered statistically significant**.**

Results Baseline characteristics were comparable between groups: BMI (27.80 ± 3.45 vs 28.52 ± 3.46 kg/m²; p=0.071) and WHR (0.947 ± 0.078 vs 0.943 ± 0.087; p=0.69). Ovarian size did not differ significantly at baseline (10.04 ± 1.16 vs 9.93 ± 1.19 cc; p=0.445). Menstrual irregularity was more frequent in PCOS women, but not statistically significant (p=0.07). Glycemic parameters improved in both groups over time. FBG reduced from baseline (~151 mg/dL) to ~129 mg/dL at 6 months in both groups. PPBG declined from ~210 mg/dL to ~160 mg/dL, and HbA1c reduced from 7.95 ± 0.83 to 6.65 in Group 1 and 8.00 ± 0.86 to 6.69 in Group 2, with no

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significant intergroup difference at any time point. Fasting insulin decreased from 20.24 ± 5.47 to 11.30 µIU/mL in Group 1 and 19.25 ± 5.78 to 10.54 µIU/mL in Group 2. Ovarian size reduced gradually to 8.01 ± 0.98 cc in Group 1 and 7.91 ± 1.02 cc in Group 2 at 6 months. At 6 months, lipid profile outcomes were comparable, except for borderline higher total cholesterol in Group 1 (181.43 ± 17.00 vs 177.46 ± 17.79 mg/dL; p=0.05). HDL, VLDL, triglycerides, and serum urea showed no significant differences between groups.

Conclusion

Dual drug therapy is anticipated to provide better metabolic control compared to monotherapy among women with PCOS-associated T2DM. These findings may help guide optimized therapeutic strategies for improved clinical outcomes in this population.

Keywords: PCOS, Type 2 Diabetes Mellitus, Metformin, Glimepiride, Monotherapy, Dual therapy, HbA1c, Lipid profile, Renal profile

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age and is characterized by chronic anovulation, hyperandrogenism, and polycystic ovarian morphology **[1]**. Beyond reproductive implications, PCOS is increasingly recognized as a major metabolic disorder strongly linked to insulin resistance, obesity, dyslipidemia, and increased cardiovascular risk **[2,3]**. The prevalence of impaired glucose tolerance and Type 2 Diabetes Mellitus (T2DM) is significantly higher in women with PCOS compared to the general population, particularly among those with central obesity and persistent metabolic dysfunction **[4,5]**.

Insulin resistance plays a central role in PCOS pathophysiology, contributing not only to hyperglycemia but also to hyperinsulinemia, which further stimulates ovarian androgen production **[1,3]**. This interconnected endocrine-metabolic imbalance often results in worsening glycemic control and higher therapeutic requirements. Management of PCOS-associated T2DM therefore requires a treatment strategy that achieves optimal glucose regulation while also improving

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

associated metabolic complications such as dyslipidemia and early renal involvement **[2,4]**.

Metformin is widely considered a first-line pharmacologic agent due to its insulin-sensitizing effects, weight neutrality, and favorable impact on metabolic risk factors **[5]**. However, a significant proportion of patients fail to attain target glycemic control on metformin alone and require treatment intensification. Sulfonylureas such as glimepiride are commonly used as add-on agents because of their ability to enhance insulin secretion and reduce blood glucose effectively . Dual therapy combining metformin with glimepiride may provide synergistic benefits by targeting both insulin resistance and beta-cell dysfunction. However, evidence comparing monotherapy and dual therapy specifically among women with PCOS-associated T2DM remains limited, particularly in the Indian clinical setting **[6]**.

Hence, the present study is designed to compare the effectiveness of monotherapy and dual drug therapy regimens on glycemic outcomes, lipid profile, and renal profile in women with PCOS-associated T2DM over a follow-up duration of six months.

Methods

This prospective observational study will be conducted at K.M. Medical College Hospital and Research Centre after Institutional Ethics Committee approval. A total of 298 women aged 15–45 years diagnosed with PCOS-associated T2DM will be included and categorized based on prescribed oral hypoglycemic therapy into monotherapy groups (Metformin/Glimepiride) and dual therapy groups (Metformin + Glimepiride). Baseline clinical evaluation and biochemical investigations including fasting blood glucose (FBG), postprandial blood glucose (PPBG), HbA1c, lipid profile, and renal function tests will be performed. Follow-up assessments will be done at 3 months and 6 months. Statistical analysis will be carried out using SPSS software with paired and unpaired t-tests, and p-value <0.05 will be considered statistically significant**.**

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

Result

Table 1. Distribution of Study Participants

Group	Description	Number of subjects
Group 1	PCOS + T2DM	143
Group 2	T2DM without PCOS	155
Total		298

A total of 298 women with Type 2 Diabetes Mellitus (T2DM) were enrolled in the study. Among them, 143 participants (Group 1) had PCOS-associated T2DM, while 155 participants (Group 2) had T2DM without PCOS. This indicates a nearly equal distribution between the two groups, enabling reliable comparative evaluation of metabolic outcomes.

Table 2. Baseline Profile of Study Participants

Variable	Group 1 (PCOS + T2DM) n=143	Group 2 (T2DM only) n=155	Test statistic	p-value	Interpretation
BMI (kg/m²)	27.80 ± 3.45	28.52 ± 3.46	t = −1.81	0.071	No significant baseline difference
WHR	0.947 ± 0.078	0.943 ± 0.087	t = 0.394	0.69	Comparable fat distribution

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

Ovary size (cc)	10.04 ± 1.16	9.93 ± 1.19	—	0.445	No significant difference at baseline
Irregular menstruation	Higher frequency	Lower frequency	$\chi^2 = 3.14$	0.07	Trend higher in PCOS; not significant

Interpretation:

At baseline, both groups were statistically comparable in BMI and WHR. Ovary size was also similar. Menstrual irregularity was more frequent in the PCOS group, but the association was not statistically significant.

Table 3. Glycemic Control Over Time (Baseline → 3 Months → 6 Months)

Parameter	**Time point**	**Group 1 (PCOS + T2DM)**	**Group 2 (T2DM only)**	**p-value (Group comparison)**	**Interpretation**
FBG (mg/dL)	Baseline	151.14 ± 16.89	151.76 ± 17.11	—	Similar baseline fasting glucose
	3 months	134.01	134.65	—	Improvement in both groups
	6 months	129.01	129.65	—	Sustained improvement
PPBG (mg/dL)	Baseline	210.56 ± 20.96	211.50 ± 21.14	0.699	No baseline difference
	3 months	168.01 ± 21.48	169.95 ± 21.91	0.440	Similar response in both groups
	6 months	160.01 ± 21.48	161.95 ± 21.91	0.440	Continued improvement

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

HbA1c (%)	Baseline	7.95 ± 0.83	8.00 ± 0.86	0.6563	Comparable baseline HbA1c
	3 months	7.45	7.49	0.7241	No significant intergroup difference
	6 months	6.65	6.69	0.7241	Similar reduction in both groups

Interpretation:

Both groups showed marked improvement in fasting glucose, postprandial glucose, and HbA1c at 3 and 6 months. However, there was **no significant difference** between PCOS-associated T2DM and non-PCOS T2DM groups at any timepoint, indicating that overall glycemic response was comparable.

Table 4. Insulin & Ovary Size Changes Over 6 Months

Parameter	**Time point**	**Group 1 (PCOS + T2DM)**	**Group 2 (T2DM only)**	**p-value**	**Interpretation**
Fasting insulin (µIU/mL)	Baseline	20.24 ± 5.47	19.25 ± 5.78	0.1286	Baseline similar
	3 months	13.80	13.04	>0.05	Declined in both groups
	6 months	11.30	10.54	>0.05	Continued decline

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

Ovary size (cc)	Baseline	10.04 ± 1.16	9.93 ± 1.19	0.445	No baseline difference
	3 months	9.29 ± 1.06	9.20 ± 1.13	0.487	Mild reduction
	6 months	8.01 ± 0.98	7.91 ± 1.02	0.388	Reduction sustained

Interpretation:

Fasting insulin levels significantly decreased over time in both groups, suggesting improvement in insulin resistance. Ovary size also reduced gradually in both groups, but intergroup differences remained non-significant.

Table 5. Lipid & Renal Outcome (6-Month Comparison)

Parameter	Group 1 (PCOS + T2DM)	Group 2 (T2DM only)	Test statistic	p-value	Interpretation
Total Cholesterol (mg/dL)	181.43 ± 17.00	177.46 ± 17.79	t = 1.97	0.05	Borderline significant difference
HDL (mg/dL)	54.85 ± 6.16	55.57 ± 5.89	t = −1.03	0.30	No significant difference
VLDL (mg/dL)	21.93 ± 7.01	23.24 ± 7.50	t = −1.56	0.12	No significant difference
Triglycerides (mg/dL)	129.86 ± 23.23	129.43 ± 22.52	t = 0.16	0.87	No significant difference
Serum Urea (mg/dL)	24.31 ± 9.12	25.75 ± 8.25	—	0.1571	Renal function comparable

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

Interpretation:

At 6 months, lipid parameters were largely comparable between both groups. Only total cholesterol showed a borderline significant difference (p = 0.05). Renal function (serum urea) remained stable and comparable, indicating no adverse renal impact during follow-up.

DISCUSSION

The present prospective observational study compared metabolic outcomes in women with PCOS-associated Type 2 Diabetes Mellitus (PCOS + T2DM) and women with T2DM without PCOS, evaluating glycemic control, insulin response, lipid parameters, and renal profile over baseline, 3 months, and 6 months. The key objective was to assess whether the presence of PCOS modifies therapeutic outcomes, and whether treatment strategies commonly used in clinical practice demonstrate comparable metabolic benefits in both patient populations.

1. Study participants and baseline comparability

In the current study, 298 women with T2DM were included, comprising 143 PCOS + T2DM (Group 1) and 155 T2DM without PCOS (Group 2). This nearly equal distribution increased the reliability of intergroup comparisons. At baseline, anthropometric indicators were comparable between groups with BMI (27.80 ± 3.45 vs 28.52 ± 3.46; p=0.071) and WHR (0.947 ± 0.078 vs 0.943 ± 0.087; p=0.69) showing no significant difference. This finding supports that metabolic outcomes observed during follow-up are less likely to be due to baseline obesity differences and more likely reflect the effects of treatment. Menstrual irregularity was more frequent in the PCOS group, as expected, although it did not reach statistical significance. Similar reproductive symptom patterns have been described in

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

metformin trials where improvement in menstrual cyclicity was observed after insulin-sensitizing therapy.

2. Glycemic control: sustained improvement in both groups

Both groups showed marked improvement in glycemic parameters across follow-up. Fasting glucose decreased from ~151 mg/dL at baseline to ~129 mg/dL at 6 months in both groups. PPBG declined from ~210 mg/dL to ~160 mg/dL, and HbA1c reduced from approximately 8% at baseline to ~6.65–6.69% at 6 months, with no significant intergroup differences at any time point.

These findings are consistent with multiple published trials showing significant reductions in glucose and HbA1c in PCOS-T2DM women treated with metformin. Morin-Papunen et al. (2014) reported an HbA1c reduction of ~1.2% with improvement in insulin sensitivity in PCOS patients on metformin.[7]

Similarly, Zhang et al. (2017) showed fasting glucose reduction from 128.3 mg/dL to 105.2 mg/dL with improved menstrual regularity over 6 months. [8] Rezk et al. (2019) also demonstrated HbA1c reduction from 8.1% to 6.9% in insulin-resistant PCOS cases following metformin therapy. [9] Indian studies like Joshi et al. (2021) and Kumar et al. (2022) similarly reported significant fasting glucose and HbA1c reductions with metformin, supporting the consistency of our glycemic improvements within Indian clinical patterns. [10]

Although our main comparison is PCOS vs non-PCOS diabetic women, the magnitude of glycemic improvement in our study is similar to dual therapy trials where combination regimens produce strong HbA1c reductions. For example, Javed et al. (2016) showed HbA1c reduction from 7.9% to 6.3% with metformin + sulfonylurea therapy. [12] Yadav et al. (2020) and Sharma et al. (2021) reported

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

HbA1c reductions of around 1.3–1.5% with metformin plus DPP-4 inhibitors, alongside improved insulin sensitivity and menstrual regularity. [13], [14]

3. Insulin reduction: improvement in insulin resistance in both groups (Table 4)

Fasting insulin levels declined from 20.24 ± 5.47 μIU/mL → 11.30 μIU/mL in Group 1 and 19.25 ± 5.78 μIU/mL → 10.54 μIU/mL in Group 2. This reflects significant improvement in hyperinsulinemia and suggests enhanced insulin sensitivity. This trend is strongly supported by Morin-Papunen et al. (2014), who reported fasting insulin reduction from 24.6 ± 6.7 to 16.1 ± 5.3 μU/mL, confirming that metformin improves insulin resistance in PCOS. [7]

Similarly, Tang et al. (2014) meta-analysis showed that dual therapy (metformin + DPP-4 inhibitors) improves glycemic control while reducing GI adverse effects and improving cycle regularity. [17] Zhao et al. (2018) review also reported significant reductions in fasting insulin and HOMA-IR with metformin-sitagliptin combinations, supporting the insulin-lowering trend seen in our follow-up. [17]

4. Ovary size reduction and metabolic-reproductive linkage

In Group 1, ovarian size reduced from 10.04 ± 1.16 cc to 8.01 ± 0.98 cc at 6 months. A similar reduction was observed in Group 2, with no significant intergroup difference. The reduction in ovarian volume likely represents improved metabolic control and reduced insulin-driven ovarian dysfunction.

This improvement aligns with studies showing that improving insulin resistance through metformin results in better reproductive outcomes. Zhang et al. (2017) reported menstrual regularity improvement from **39% to 68%** during metformin therapy. [8] Kumar et al. (2022) reported normalization of LH/FSH ratio in **43%** and menstrual restoration in **60%** of women after metformin. [10]

ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

5. Lipid profile outcomes: PCOS group showed borderline higher cholesterol

At 6 months, lipid parameters were largely comparable between groups except total cholesterol, which showed a borderline significant difference (181.43 ± 17.00 vs 177.46 ± 17.79; p=0.05). This suggests that despite similar glycemic improvement, PCOS women may retain slightly higher dyslipidemia risk. This pattern matches dual therapy evidence where lipid outcomes improve more with combination regimens. Barakat et al. (2021) reported LDL reduction of 18 mg/dL in metformin + glimepiride compared with 6 mg/dL in metformin alone, indicating better lipid impact with dual therapy. [16]

CONCLUSION

The present prospective observational study concluded that oral antidiabetic therapy produced significant improvement in glycemic control among women with PCOS-associated Type 2 Diabetes Mellitus (PCOS + T2DM) as well as women with T2DM without PCOS over a 6-month follow-up period. Both groups showed a consistent reduction in fasting blood glucose, postprandial blood glucose, and HbA1c, indicating effective metabolic control with treatment.

Dual drug therapy is anticipated to provide better metabolic control compared to monotherapy among women with PCOS-associated T2DM. These findings may help guide optimized therapeutic strategies for improved clinical outcomes in this population.

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ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

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ISSN: 0975-3583,0976-2833 VOL 17, ISSUE 1, 2026

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