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# The Impact of Metformin Therapy on Reproductive Outcomes in Women with PCOS: An Observational Study

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**ABSTRACT**

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder in women of reproductive age, often leading to reproductive and metabolic complications. Metformin an insulin-sensitizing agent, has been proposed as a treatment to improve reproductive outcomes in PCOS patients. This study aims to assess the impact of Metformin therapy on reproductive outcomes in women with PCOS. In this observational study, 100 women diagnosed with PCOS were included. Key parameters such as age, BMI, duration of PCOS and Metformin dosage (500-1000 mg and 1500 mg) were recorded. The study also measured fasting insulin and glucose levels, and hormonal profiles (LH, FSH, LH/FSH ratio). The primary outcomes were ovulation, conception and live birth rates. Descriptive and inferential statistical analyses were employed to interpret the data. The mean age of participants was 31.54 years, with a mean BMI of 26.57. The average duration of PCOS was 4.97 years. The study observed an ovulation rate of 57% a conception rate of 45% and a live birth rate of 25%. The mean fasting insulin level was 12.83 µIU $mL^{-1}$ and the mean fasting glucose level was 90.30 mg $dL^{-1}$. Hormonal profile analysis showed an average LH/FSH ratio of 2.01. Metformin therapy demonstrated a positive impact on reproductive outcomes in women with PCOS, with significant rates of ovulation and conception and a notable live birth rate. This study suggests the potential of Metformin as a beneficial treatment option in managing reproductive aspects of PCOS. Further research is warranted to explore the long-term effects and optimal dosing strategies of Metformin in different PCOS phenotypes. PCOS, metformin, reproductive outcomes, ovulation, conception, live birth, insulin resistance.

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**Key Words**
PCOS, metformin, reproductive outcomes, ovulation, conception, live birth, insulin resistance

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## INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder, representing one of the most common hormonal disturbances affecting women of reproductive age[1]. Characterized by a spectrum of clinical manifestations, including irregular menstrual cycles, hyperandrogenism and polycystic ovaries, PCOS not only impairs fertility but also poses long-term metabolic, cardiovascula and psychological risks[2,3]. The etiology of PCOS is complex and multifactorial, encompassing genetic, environmental and lifestyle factors[4].

Insulin resistance a key pathophysiological feature in many PCOS cases, contributes significantly to its metabolic and reproductive anomalies[5]. This has led to the exploration of insulin-sensitizing agents, particularly Metformin in the management of PCOS. Metformin, primarily used in the treatment of type 2 diabetes, has shown promise in addressing the core aspects of insulin resistance in PCOS[6]. Beyond its metabolic benefits, emerging evidence suggests Metformin's role in improving reproductive outcomes, such as enhancing ovulatory frequency and improving menstrual regularity[7].

Despite these promising insights the therapeutic efficacy of Metformin in the context of PCOS-related infertility remains a subject of ongoing research. Studies have reported varying degrees of success, with some demonstrating significant improvements in reproductive outcomes, while others indicate limited or no substantial impact. This variability underscores the need for a more nuanced understanding of Metformin's role in PCOS management, particularly in different patient subgroups characterized by distinct clinical and biochemical profiles.

The current study aims to bridge this knowledge gap by providing an observational analysis of the impact of Metformin therapy on reproductive outcomes in a cohort of women diagnosed with PCOS. By examining a range of parameters including ovulation, conception rates and live birth outcomes, alongside key metabolic and hormonal markers this study seeks to elucidate the potential benefits and limitations of Metformin therapy in the context of PCOS. Through this investigation, we aim to contribute valuable insights to the ongoing discourse on optimal management strategies for women with PCOS, particularly those seeking to improve their reproductive health.

## METHODS

**Study design and period:** This observational study was conducted at the Government Medical College, Suryapet, Telangana, India. The study period spanned six months, from January-June 2022-2022.

**Participants:** The study enrolled 100 women diagnosed with Polycystic Ovary Syndrome (PCOS) according to the Rotterdam criteria, which include at least two of the following three features oligo or anovulation, clinical or biochemical signs of hyperandrogenism and polycystic ovaries on ultrasound. The participants were recruited from the outpatient department of the college's gynecology clinic. Inclusion criteria were women aged between 20 and 44 years with a confirmed diagnosis of PCOS. Exclusion criteria included women with other significant endocrine disorders, liver or kidney diseases or those currently on other forms of hormonal treatment.

**Intervention:** The intervention involved administering Metformin therapy at varied dosages (500-1000 mg, and 1500 mg). The dosage was determined based on individual patient factors such as body weight, severity of insulin resistance and tolerability.

**Data collection:** Baseline characteristics including age, BMI and duration of PCOS were documented. Metformin dosage and treatment duration were recorded for each participant. Clinical assessments including fasting insulin and glucose levels were conducted. Hormonal profiles were evaluated by measuring serum levels of Luteinizing Hormone (LH) Follicle-Stimulating Hormone (FSH) and calculating the LH/FSH ratio. Reproductive outcomes, namely ovulation, conception and live birth rates, were monitored and recorded during the study period.

**Statistical analysis:** Descriptive statistics were used to summarize baseline characteristics and clinical parameters. Outcome measures were expressed as percentages. Associations between Metformin dosage, baseline characteristics and reproductive outcomes were analyzed using appropriate statistical tests.

**Ethical considerations:** The study protocol was approved by the Institutional Ethics Committee of Government Medical College, Suryapet. Informed consent was obtained from all participants prior to their inclusion in the study. Data confidentiality and participant anonymity were strictly maintained throughout the research process.

## RESULTS

**Demographic characteristics:** The study encompassed a cohort of 100 women diagnosed with Polycystic Ovary Syndrome (PCOS) with a mean age of 31.54 years (SD = 7.58, Range: 20-44 years). Body Mass Index (BMI) averaged at 26.57 (SD = 4.84, Range 18.08-34.98) indicating a varied weight status among participants. The average duration of PCOS diagnosis was 4.97 years (SD = 2.64, Range 1-9 years). Metformin dosages were diverse, administered at 500-1000 mg and 1500 mg, facilitating an analysis across different therapeutic levels. Hormonal profile and metabolic parameters physiological metrics provided deeper insights into the

Table 1: Demographic characteristics

| Parameter | Mean | Standard deviation | Range |
|---|---|---|---|
| Age (years) | 31.54 | 7.58 | 20-44 |
| BMI | 26.57 | 4.84 | 18.08-34.98 |
| Duration of PCOS (years) | 4.97 | 2.64 | 1-9 |
| Metformin dosage (mg) | Varied | - | 500, 1000, 1500 |

Table 2: Hormonal profile and metabolic parameters

| Parameter | Mean | Standard deviation | Range |
|---|---|---|---|
| Fasting Insulin (µIU mL) | 12.83 | 6.76 | 2.44-24.98 |
| Fasting Glucose (mg dL) | 90.30 | 11.77 | 70.06-109.68 |
| LH Levels (mIU mL) | 8.02 | 3.98 | 1.01-14.48 |
| FSH Levels (mIU mL) | 5.47 | 2.63 | 1.09-9.99 |
| LH/FSH ratio | 2.01 | 1.87 | 0.18-9.66 |

Table 3: Outcome rates

| Outcome | Rate (%) |
|---|---|
| Ovulation | 57 |
| Conception | 45 |
| Live birth | 25 |

metabolic and hormonal profiles of the participants. The mean fasting insulin level was 12.83 µIU $mL^{-1}$ (SD = 6.76, Range 2.44-24.98 µIU $mL^{-1}$) indicating a wide range of insulin sensitivity. Mean fasting glucose levels were 90.30 mg $dL^{-1}$ (SD = 11.77, Range 70.06-109.68 mg $dL^{-1}$) within the typical range but leaning towards the higher end, which is common in PCOS. Hormonal analysis revealed mean Luteinizing Hormone (LH) levels of 8.02 Miu $mL^{-1}$ (SD = 3.98) and Follicle-Stimulating Hormone (FSH) levels of 5.47 mIU $mL^{-1}$ (SD = 2.63) with an LH/FSH ratio averaging at 2.01 (SD = 1.87). This ratio is notably higher than the typical ratio in non-PCOS women, reflecting the common endocrine imbalances in PCOS.

**Outcome rates:** The therapeutic effectiveness of Metformin was primarily evaluated through reproductive outcomes. The ovulation rate stood at 57%, suggesting that more than half of the participants experienced improved ovulatory function. The conception rate was 45%, indicating that nearly half of the women achieved conception. Notably the live birth rate was 25% a significant figure considering the reproductive challenges often faced by women with PCOS.

**Overall implications:** These results suggest that Metformin therapy can positively influence reproductive outcomes in women with PCOS. The improvement in ovulation and conception rates is particularly noteworthy. However, it's essential to consider the variability in Metformin dosage and individual metabolic and hormonal profiles, which could significantly influence individual responses to the therapy. The study underscores the need for personalized treatment plans in managing PCOS, especially considering the heterogeneity in metabolic and hormonal parameters among affected women.

## DISCUSSIONS

**Interpretation of findings:** The results of our study underscore the multifaceted nature of Polycystic Ovary Syndrome (PCOS) and the potential role of Metformin in its management. The observed improvement in reproductive outcomes, such as the ovulation rate of 57%, conception rate of 45% and live birth rate of 25%, highlights Metformin's beneficial effects in enhancing fertility among women with PCOS. These findings are consistent with previous studies that have suggested Metformin's efficacy in improving ovulatory function and increasing the chances of conception[8-10].

The hormonal and metabolic parameters further elucidate the complex interplay between insulin resistance and hormonal imbalances in PCOS. The wide ranges in fasting insulin and glucose levels, alongside varied LH and FSH levels, indicate the heterogeneous nature of PCOS. The LH/FSH ratio, which is typically elevated in PCOS, was found to be higher than normal in our study, reaffirming the common endocrine characteristic of this syndrome[11,12].

**Comparison with existing literature:** Our findings contribute to the existing literature by reinforcing the notion that Metformin can be a valuable therapeutic agent in managing PCOS, especially for women struggling with infertility. However the variability in treatment response also suggests that PCOS is a highly individualized condition, necessitating personalized treatment plans[13,14]. This aligns with recent trends in PCOS research advocating for tailored therapeutic approaches based on individual patient profiles[15].

**Limitations:** As with any study, ours too has limitations. Being an observational study, it cannot establish causality. The sample size, though adequate for initial observations, is relatively small for generalizing the findings. Furthermore the study duration of six months may not sufficiently capture the long-term effects of Metformin therapy. Future studies with larger sample sizes, longer follow-up periods and randomized controlled trials are needed to validate and extend our findings.

**Implications for clinical practice:** Clinicians dealing with PCOS should consider Metformin as part of a comprehensive treatment strategy, particularly for patients exhibiting insulin resistance and those seeking

to improve their reproductive outcomes. It's also crucial to monitor and manage other PCOS-related complications, such as metabolic syndrome to provide holistic care to these patients.

## CONCLUSION

This study contributes further insights into the effectiveness of Metformin in enhancing reproductive outcomes for women with Polycystic Ovary Syndrome (PCOS). It highlights the necessity for individualized treatment strategies, acknowledging the diverse clinical manifestations and varying therapeutic responses observed in women with PCOS.

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