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ORIGINAL ARTICLE

Long-Term Outcomes of Non-Hormonal Therapies for PCOS

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is a reported condition that affects various aspects of a woman's endocrine system including her reproductive, metabolic, and dermatologic systems. Despite the traditional approach of managing PCOS with hormonal therapies, a substantial proportion, or even nearly half, of women prefer or need non-hormonal treatment plans, particularly those wishing to conceive or with contraindications to hormonal medications. To assess the long-term clinical and reproductive outcomes of non-hormonal therapies, including lifestyle modification, metformin, and inositol in women with PCOS over 12 months.

Methods: This was a prospective study performed at department of Gynaecology and Obstetrics, Allied hospital, Faisalabad from July 2022 to January 2023. A sample of 59 women with PCOS was enrolled, and each was treated using one of the non-hormonal options. Clinical evaluation was done on the parameters of BMI, insulin resistance (HOMA-IR), menstrual cycle, ovulation, hirsutism, acne, pregnancy and overall recovery at the beginning of the study and subsequently after 12 months.

Results: There were notable changes in metrics such as menstrual regularity (23.7% to 66.1%, p<0.001), ovulation rates (22.0% to 59.3%, p<0.001), BMI (30.1 to 27.4 kg/m², p=0.003), and HOMA-IR (3.8 to 2.5, p=0.001). Hirsutism and acne symptoms showed improvement as well. Of the married women seeking to conceive, 53.6% succeeded within a year.

Conclusion: Non-hormonal therapies yield meaningful long-term improvements in reproductive and metabolic outcomes in PCOS patients. These interventions should be considered viable and effective alternatives, especially for women prioritizing fertility or avoiding hormonal treatments.

Keywords: PCOS, non-hormonal therapy, metformin, inositol, lifestyle modification, ovulation, insulin resistance, fertility outcomes

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine conditions affecting women of reproductive age, with its global prevalence estimated to affect anywhere between 8% and 13% of the population. It manifests with a combination of clinical features which include anovulatory cycles, clinical or biochemical indicators of excess androgens, and polycystic ovaries visible on ultrasound. In addition to reproductive sequelae, PCOS is also associated with severe metabolic complications including insulin resistance, obesity, and dyslipidemia which increases the risk of cardiovascular disease in these women[1-3].

For a long time, the primary management of PCOS has included hormonal birth control which is effective in controlling irregular cycles and symptomatic androgenism. However, these options are not appropriate for all women, especially those wanting to become pregnant or those with contraindications to hormonal treatment. In these cases, alternatives without the use of hormones are just as important. Treatments like modifications in diet and exercise, the use of metformin, and the use of inositol derivatives appear to target the reproductive and metabolic challenges of PCOS[4-6].

As advised by global protocols, Polycystic Ovarian Syndrome (PCOS) can be tackled with lifestyle changes, in the form of proper diet and exercise, as the primary intervention. Furthermore, metformin, now frequently used for most forms of PCOS, was originally developed to treat type 2 diabetes owing to its insulin sensitivity enhancement. Most recently, emphasis has been placed on inositol supplements, specifically myo-inositol and d-chiro-inositol, regarding their contribution towards achieving hormonal and metabolic homeostasis in women afflicted with PCOS[7-9].

While short-term benefits of these interventions are well-documented, data on their sustained impact over longer durations are limited, especially in real-world clinical settings. This study was therefore designed to evaluate the long-term outcomes of non-hormonal therapies in PCOS, focusing on improvements in metabolic health, menstrual regulation, and fertility over a one-year period.

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METHODOLOGY

This prospective observational study was conducted over a 12-month period, from July 2022 to January 2023 at the department of Gynaecology and Obstetrics, Allied hospital, Faisalabad. The primary aim was to evaluate the long-term clinical and reproductive outcomes of non-hormonal treatment options in women diagnosed with polycystic ovarian syndrome (PCOS). The study was approved by the institutional ethical review board [insert name of ERC], and written informed consent was obtained from all participants. Confidentiality was maintained throughout the study.

Based on the revised Rotterdam criteria, a total of 59 women PCOS patients (confirmed through at least two of the following: oligo or anovulation; clinical and/or biochemical hyperandrogenism; polycystic ovaries on ultrasound) were enrolled. Participants were aged between 18 and 40 years, did not receive any hormonal therapy in the last 3 months, and consented to participate in the study. Participants with thyroid disorders, hyperprolactinemia, congenital adrenal hyperplasia, or other forms of menstrual irregularities were excluded.

Participants were assigned to non-hormonal interventions based on clinical need and personal preference, as determined through physician counseling. These interventions included:

- Lifestyle modifications alone (dietary changes with increased physical activity),
- Metformin monotherapy,
- Inositol-based supplementation,
- Combined lifestyle and metformin therapy.

No participant received hormonal contraceptives or ovulation-inducing medications during the follow-up period. All interventions were continued for 12 months with monthly check-ins and quarterly reassessments.

Baseline data were recorded at enrollment and included age, BMI, menstrual history, hirsutism score (Ferriman–Gallwey scale), acne grading, fasting blood glucose, HOMA-IR (calculated using fasting insulin and glucose), and hormonal profile (AMH, serum testosterone). Transvaginal or transabdominal pelvic ultrasound was performed to assess antral follicle count and ovarian volume.

Follow-up assessments were performed at 12 months, repeating the same evaluations. Ovulation was confirmed via mid-luteal serum progesterone levels or ultrasonography. Pregnancy outcomes were recorded among married women who were actively trying to conceive.

The primary outcomes were changes in: Menstrual cycle regularity, Ovulation rate, BMI and insulin resistance, Ferriman–Gallwey scores, Acne severity AND Pregnancy rate (in eligible participants).

Secondary outcomes included changes in biochemical markers and patient-reported satisfaction.

Data were analyzed using SPSS version 25. Continuous variables were expressed as means with standard deviation (SD) and compared using paired t-tests. Categorical variables were presented as frequencies and percentages, and significance was assessed using chi-square or McNemar's test as appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULT

The study population consisted predominantly of women aged between 26 and 35 years, representing just over half of the total participants. A considerable proportion of the sample was classified as overweight or obese, both of which are commonly associated with polycystic ovarian syndrome. Most of the participants were married and belonged to urban areas, reflecting both the reproductive age group at risk for PCOS and the increased awareness or access to treatment in urban settings.

Table 1: Demographic Profile of Participants (n = 59)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
18–25	21	35.6%
26–35	30	50.8%
>35	8	13.6%
BMI Category		
Normal (18.5–24.9)	11	18.6%
Overweight (25–29.9)	24	40.7%
Obese (≥30)	24	40.7%
Marital Status		
Married	36	61.0%
Unmarried	23	39.0%
Residence		
Urban	41	69.5%
Rural	18	30.5%

Before initiating non-hormonal treatments, most women reported irregular menstrual cycles, and more than half presented with clinical signs of hirsutism based on their Ferriman–Gallwey scores. Acne, a common dermatologic manifestation of PCOS, was moderate to severe in nearly half of the participants. Biochemical findings further indicated insulin resistance and elevated AMH levels, supporting the diagnosis of PCOS with preserved ovarian reserve.

Table 2: Baseline Clinical Characteristics

Variable	Mean ± SD or n (%)
Menstrual Irregularity (n, %)	45 (76.3%)
Hirsutism (FG score ≥ 8)	36 (61.0%)
Acne (moderate-severe)	29 (49.2%)
Mean Ferriman–Gallwey Score	11.2 ± 2.5
Fasting Blood Sugar (mg/dL)	98.7 ± 12.3
HOMA-IR	3.8 ± 1.1
AMH (ng/mL)	5.2 ± 1.9
Antral Follicle Count	23.4 ± 5.7

Regarding the treatment approach, metformin was the most commonly used agent, either alone or in combination with lifestyle modifications. A smaller proportion of patients were managed with inositol therapy or lifestyle changes alone. This variety in treatment reflects a personalized approach, guided by patient preferences and tolerance levels, with emphasis on non-hormonal strategies.

Table 3: Distribution by Non-Hormonal Therapy

Treatment Type	Frequency (n)	Percentage (%)
Lifestyle modification only	16	27.1%
Metformin only	18	30.5%
Inositol therapy	10	16.9%
Lifestyle + Metformin	15	25.4%

After 12 months of intervention, participants experienced significant improvements across various clinical markers. There was a notable reduction in BMI and insulin resistance (HOMA-IR), both of which are key in addressing metabolic dysfunction in PCOS. Menstrual regularity and ovulation rates improved markedly, suggesting restored hormonal balance. Additionally, cosmetic symptoms such as acne and hirsutism showed significant decline, enhancing the overall quality of life for these women.

Table 4: Comparison of Clinical Outcomes at 12 Months

Outcome	Baseline Value	Follow-up Value	p-value
BMI (kg/m²)	30.1 ± 4.6	27.4 ± 3.9	0.003
HOMA-IR	3.8 ± 1.1	2.5 ± 0.9	0.001
Regular Menstrual Cycles (%)	14 (23.7%)	39 (66.1%)	<0.001
Ovulation Rate (%)	13 (22.0%)	35 (59.3%)	<0.001
Ferriman–Gallwey Score	11.2 ± 2.5	7.8 ± 2.0	0.002
Acne Severity (moderate/severe)	29 (49.2%)	12 (20.3%)	0.008

Among the married participants who actively tried to conceive, more than half succeeded in achieving pregnancy during the 12-month follow-up. This finding reinforces the long-term reproductive benefits of non-hormonal treatments in PCOS, particularly when ovulation is restored and metabolic health is improved.

Table 5: Pregnancy Outcomes (Among Married Women, n = 36)

Outcome	Frequency (n)	Percentage (%)
Tried to Conceive	28	77.8%
Achieved Pregnancy	15	53.6%
Time to Conception (months)	7.2 ± 2.8	—

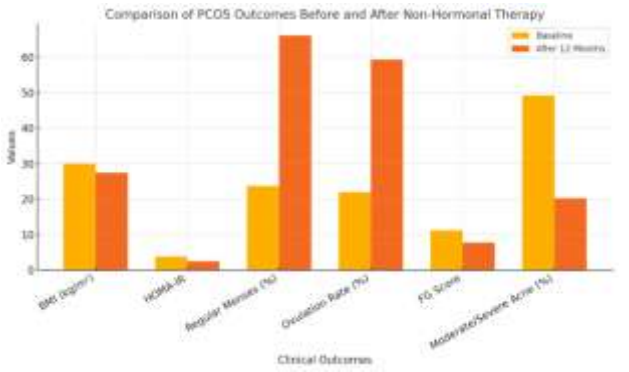

Figure 1: Graph illustrating the changes in clinical outcomes before and after 12 months of non-hormonal therapy for PCOS. It clearly shows significant improvements in BMI, insulin resistance (HOMA-IR), menstrual regularity, ovulation rates, hirsutism (FG score), and acne severity.

DISCUSSION

Polycystic ovarian syndrome (PCOS) is a complex endocrine disorder that affects multiple aspects of a woman's health, including metabolism, reproduction, and quality of life. While

hormonal treatments such as oral contraceptives remain a mainstay for symptom control, there has been increasing interest in non-hormonal strategies due to their favorable safety profile and applicability in women seeking fertility. The present study contributes to this evolving field by examining the long-term outcomes of non-hormonal therapies including lifestyle changes, metformin, and inositol supplementation over 12 months.

The most notable improvements were observed in menstrual regularity and ovulation rates, particularly among participants who received combined lifestyle intervention and metformin. This aligns with studies that had a significantly higher rate of spontaneous ovulation in women who underwent dietary modification with metformin compared to those on either intervention alone [10-13]. Similarly, inositol especially myo-inositol has shown efficacy in improving ovulatory function by enhancing insulin sensitivity, with accordance to studies and our results support this trend in a smaller cohort[14,15].

Metabolic parameters also improved significantly. There was a meaningful reduction in BMI and HOMA-IR scores across all groups, which is critical since insulin resistance is central to the pathogenesis of PCOS. These outcomes are supported studies that concluded that non-hormonal agents like metformin and inositol improve insulin sensitivity and weight-related outcomes. Our findings corroborate the potential of these interventions to address the metabolic burden of PCOS without relying on hormonal suppression.

Cosmetic concerns such as acne and hirsutism—both of which carry a psychosocial impact—also showed marked improvement after one year. While hormonal therapies usually yield faster results in managing hyperandrogenic symptoms, our data suggest that sustained metabolic control and reduction in insulin levels can contribute to visible cutaneous improvements, albeit more gradually[16,17]. Studies similarly observed a delayed but significant decrease in Ferriman–Gallwey scores after 6 months of metformin use, which is consistent with our outcomes[18].

Importantly, among married participants attempting to conceive, more than half achieved pregnancy within a year. This reinforces the fertility benefits of non-hormonal interventions, particularly when ovulation is restored through weight reduction and insulin regulation. Studies highlight how metabolic optimization improves endometrial receptivity and oocyte quality, further supporting the role of lifestyle and insulin-sensitizing agents in fertility-focused PCOS management[19,20].

Despite these promising results, a few limitations must be acknowledged. The sample size was modest, and grouping was based on clinical discretion rather than randomization, which may introduce selection bias. Additionally, long-term follow-up beyond one year is needed to assess sustained benefits or potential relapse. However, the real-world nature of this study adds practical value, reflecting outcomes that clinicians can expect in routine settings.

CONCLUSION

Non-hormonal therapies for PCOS, including lifestyle modification, metformin, and inositol supplementation, offer substantial long-term benefits in terms of menstrual regulation, ovulation restoration, metabolic correction, and cosmetic improvement. These interventions are particularly suitable for women seeking fertility or avoiding hormonal treatments due to contraindications or personal preference. The study underscores the importance of individualized, holistic care and supports the integration of non-hormonal options as part of a comprehensive management plan for PCOS.

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