

## Comparing the Effects of N-Acetylcysteine and Metformin on Biochemical and Clinical Parameters in Women with Polycystic Ovarian Syndrome at a Tertiary Care Hospital

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### Abstract:

**Background:** Polycystic Ovarian Syndrome (PCOS) is a prevalent endocrine disorder among women of reproductive age featuring insulin resistance and hormonal imbalances. Due to gastrointestinal issues caused by metformin, alternatives like N-acetylcysteine (NAC) are being explored.

**Objective:** The study assessed the effectiveness of NAC compared to metformin in treating PCOS symptoms at a tertiary care hospital.

**Methods:** In this randomized controlled trial, 80 women with PCOS were divided into NAC and metformin groups from November 2022 to March 2024. The study monitored changes in insulin resistance, hormonal profiles, menstrual regularity, ovulation rates, quality of life, BMI, and lipid profiles. Adverse effects and discontinuation rates were also recorded.

**Results:** Both treatments significantly improved insulin resistance and hormonal profiles. NAC was particularly effective in reducing insulin resistance and androstenedione levels. Menstrual and ovulation improvements were similar across both groups. NAC users experienced greater emotional well-being and fewer body hair issues along with lesser gastrointestinal side effects and discontinuation rates.

**Conclusion:** NAC might be a preferable alternative to metformin for managing PCOS, offering better tolerability and improved quality of life. Further studies are needed to validate these results and assess long-term benefits.

**Keywords:** PCOS, N-acetylcysteine, Metformin, Insulin Resistance, Hormonal Balance, Quality Of Life.

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### Introduction

Polycystic Ovarian Syndrome (PCOS) affects about 10% of women of reproductive age and presents with symptoms like irregular menstrual cycles, hyperandrogenism, and polycystic ovaries [1]. Managing PCOS involves a comprehensive approach aimed at enhancing both reproductive and metabolic outcomes [2]. Metformin, a widely used antihyperglycemic agent from the biguanide class, is favored for its effectiveness in improving insulin resistance, hormonal balance, and ovulation rates. However, due to gastrointestinal side effects and other contraindications, metformin is not suitable for all patients [3].

As an alternative, N-acetylcysteine (NAC), an antioxidant and cysteine precursor, has shown potential in improving insulin resistance and hormonal conditions in women with PCOS as evidenced by various clinical trials [4]. The

comparative study of NAC and metformin in treating PCOS is crucial for determining their relative effectiveness in amending the disorder's biochemical and clinical parameters [5]. This study, conducted at a tertiary care hospital, evaluates the efficacy of NAC and metformin in addressing insulin resistance, hormonal profiles, menstrual regularity, and overall reproductive health. It also examines their impact on quality of life and metabolic health, offering insights that could lead to more personalized and effective PCOS treatment strategies [6]. This analysis aims to refine the therapeutic roles of NAC and metformin, potentially influencing future clinical guidelines and research in PCOS management.

## Material and Methodology

This study utilized a randomized controlled trial design to assess the efficacy of N-acetylcysteine (NAC) versus metformin in managing polycystic ovarian syndrome (PCOS) at a tertiary care hospital running from November 2022 to March 2024. It involved eighty female patients who met the Rotterdam criteria for PCOS, aged between 18 and 45 years, diagnosed based on clinical signs like hirsutism, acne or alopecia, elevated androgen levels, and the presence of polycystic ovaries on ultrasound.

Participants were randomly assigned to two groups of forty each: one receiving NAC (1200 mg/day) and the other receiving metformin (1500 mg/day) following the dosages prescribed by current clinical guidelines and best practices for each treatment respectively. The study was conducted in a double-blind manner where neither the participants nor the researchers knew the treatment assignments until the study concluded.

Treatment protocols involved administering NAC and metformin orally twice daily for a duration of six months, with dosages adjusted based on initial assessments and participant tolerance. The primary outcome measures included changes in insulin resistance as measured by the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), hormonal profiles (testosterone, androstenedione, and SHBG), menstrual regularity, and ovulation rates based on patient self-reports and periodic hormonal evaluations. Secondary outcomes focused on quality of life assessed using the PCOS Quality of Life Questionnaire (PCOSQ) and metabolic parameters such as body mass index (BMI), lipid profiles, and glucose tolerance.

Data were collected at baseline, every six months during the treatment period, and at the study's conclusion, with statistical analyses conducted using the latest SPSS software. Comparative analyses between the groups were performed using independent t-tests or Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables, considering a p-value of less than 0.05 as statistically significant. This comprehensive approach aimed to provide a thorough understanding of the comparative effectiveness of NAC and metformin in the management of PCOS.

## Results

The study involved 80 women diagnosed with polycystic ovarian syndrome (PCOS) evenly divided into two treatment groups: 40 received N-

acetylcysteine (NAC) and 40 were treated with metformin. The average age of participants was 29.4 years (SD  $\pm$  4.3) with similar baseline characteristics between the groups including body mass index (BMI), insulin levels, and hormonal profiles.

Regarding insulin resistance and hormonal profiles, both groups experienced a statistically significant reduction in HOMA-IR scores, with the NAC group showing a more notable decrease in insulin resistance than the metformin group ( $p < 0.05$ ). Both treatments effectively lowered serum testosterone levels comparably across groups. Androstenedione levels saw a significant decrease in the NAC group compared to the metformin group ( $p < 0.05$ ), while SHBG levels rose in both groups without a significant difference between them.

In terms of menstrual regularity and ovulation rates, 65% of the NAC group saw improvements in menstrual regularity versus 55% in the metformin group, although this difference was not statistically significant ( $p > 0.05$ ). Ovulation rates, assessed via mid-cycle ultrasound and serum progesterone levels, improved in both groups with no significant difference noted between them.

Quality of life, assessed using the PCOS Quality of Life Questionnaire (PCOSQ), showed improvement in both groups. Notably, the NAC group experienced more significant enhancements, especially in emotional well-being and body hair symptoms ( $p < 0.05$ ). Metabolic parameters such as BMI and lipid profiles improved for all participants, with the NAC group showing a slightly better increase in HDL cholesterol levels, although this difference was not statistically significant ( $p > 0.05$ ).

In terms of adverse effects, participants in the NAC group reported mild side effects including gastrointestinal discomfort and headaches. Conversely, the metformin group encountered a higher incidence of gastrointestinal issues such as nausea and diarrhea, which led to a greater discontinuation rate among these participants.

Overall, the study concluded that both N-acetylcysteine and metformin effectively improve insulin resistance, hormonal profiles, and menstrual regularity in women with PCOS. NAC demonstrated a potentially better tolerability profile and greater improvements in quality of life. Further large-scale studies are recommended to confirm these findings and to evaluate the long-term impacts of NAC compared to metformin in managing PCOS.

**Table 1: This table presents the changes in clinical and biochemical parameters between baseline and post-treatment for both groups as well as comparative statistics where applicable.**

Parameter	NAC Group (n=40)	Metformin Group (n=40)	P-value
Average Age (years)	29.4 ( $\pm$ 4.3)	29.2 ( $\pm$ 4.5)	-
Insulin Resistance (HOMA-IR)			
Baseline	3.2	3.1	-
Post-Treatment	2.1	2.5	<0.05
Serum Testosterone (nmol/L)			
Baseline	2.9	2.8	-
Post-Treatment	2.0	2.1	>0.05
Serum Androstenedione (ng/mL)			
Baseline	2.5	2.6	-
Post-Treatment	1.8	2.2	<0.05
SHBG (nmol/L)			
Baseline	25	26	-
Post-Treatment	32	31	>0.05
Menstrual Regularity Improvement			
Improved	65%	55%	>0.05
Ovulation Rate Improvement			
Improved	72%	68%	>0.05
PCOSQ Score Improvement			
Baseline	30	31	-
Post-Treatment	45	40	<0.05
BMI (kg/m <sup>2</sup> )			
Baseline	28.5	28.7	-
Post-Treatment	27.0	27.5	>0.05
Lipid Profile - HDL (mg/dL)			
Baseline	48	47	-
Post-Treatment	52	50	>0.05
Adverse Effects			
Reported	Mild GI discomfort, headache	Nausea, diarrhea	-
Discontinuation Rate	5%	15%	<0.05

## Discussion

This study aimed to compare the efficacy of N-acetylcysteine (NAC) and metformin in improving clinical and biochemical parameters in women with polycystic ovarian syndrome (PCOS). Both treatments significantly reduced insulin resistance as measured by HOMA-IR, consistent with previous research (Smith et al. 2021; Jones & Smith 2020), although NAC showed a slightly greater effect, suggesting additional mechanisms at play. Our findings align with Lee et al. (2019), indicating that both metformin and NAC reduce androgen levels in PCOS patients, with a more pronounced decrease in androstenedione in the NAC group. This points to NAC's potent antioxidant properties possibly influencing steroidogenesis (Brown et al. 2018) [7,8, 9].

Similar to O'Connor et al. (2020), we observed improvements in menstrual regularity and ovulation rates, although the differences between NAC and metformin were not statistically significant. However, the trend favors NAC, which may be important in clinical scenarios where

patient preferences or tolerance to side effects are considered [10,11,12].

NAC's benefits extended to quality-of-life improvements, particularly in emotional and body hair domains, echoing Green et al. (2022) on the role of antioxidants in mitigating oxidative stress and inflammation associated with PCOS symptoms. The NAC group experienced fewer discontinuations and milder side effects compared to the metformin group, which is often criticized for its gastrointestinal disturbances (Davis et al. 2021). This could make NAC a preferable option for the long-term management of PCOS, especially for those sensitive to metformin's side effects.

While the study offers valuable insights, it has limitations including a small sample size and a short duration, which may not fully capture the long-term effects and sustainability of benefits from NAC and metformin. Further research with larger cohorts and extended follow-ups is necessary to confirm these findings and explore NAC's mechanistic roles in treating PCOS [13,14,15].

## Conclusion

N-acetylcysteine (NAC) and metformin are effective in managing the biochemical and clinical parameters of polycystic ovarian syndrome (PCOS). However, NAC has the advantage of a more favorable side effect profile and improved impacts on quality of life, making it a potentially better option for long-term management. These results indicate that clinicians should tailor PCOS management strategies to individual patient needs and preferences. Moreover, the findings underscore the need for additional research to fully explore NAC's therapeutic potential in treating PCOS.

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