

# Awareness of Saudi Women on Metformin Indications for Polycystic Ovary Syndrome (PCOS)

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### **Abstract**

**Objective:** This study's objective was to evaluate the awareness of Saudi women concerning the indications for the usage of Metformin in managing PCOS. It is the first-line treatment for managing insulin resistance-associated PCOS. Its underutilization stems from a lack of awareness among patients.

**Methods:** This cross-sectional study included women of reproductive age in Saudi Arabia. Copies of the electronic survey were distributed to the target population. The study was conducted over 2 months, November and December 2024.

**Results:** The study included 436 participants from Saudi Arabia. 38.8% were 20 - 30 years old. 82.1% recognized the importance of lifestyle changes for lowering insulin levels. While 36% were aware of metformin, 47.9% had not heard of it. 49.7% agreed that metformin might lower the chance of type 2 diabetes in women with PCOS, and 54.3% believed that it could help maintain regular menstrual cycles. Among the participants, 14.9% reported not using metformin, citing forgetfulness, side effects, and financial issues as barriers.

**Conclusion:** The majority of women had limited knowledge and understanding of this treatment. While most women with PCOS were aware of metformin as a medication, they lacked detailed information about its specific indications and benefits for managing PCOS. Many women did not know that metformin could help regulate menstrual cycles, improve insulin resistance, and potentially assist with weight management, which are key treatment goals for PCOS.

Keywords: Metformin; Polycystic ovarian syndrome; PCOS; Women; Saudi Arabia

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## **Abbreviations**

PCOS: Polycystic Ovary Syndrome; AES: Androgen Excess Society; HPO: Hypothalamic-Pituitary-Ovarian; AMPK: Adenosine Monophosphate Kinase; SPSS: Statistical Package for the Social Sciences; GnRH: Gonadotropin-Releasing Hormone; LH: Luteinizing Hormone

## Introduction

Polycystic Ovarian Syndrome (PCOS) is a complex endocrine disorder predominantly affecting females of reproductive age and is characterized by a range of clinical and metabolic disturbances [1]. The syndrome is often associated with anovulation, hyperandrogenism, insulin resistance, and related metabolic disorders, which contribute to various health issues, including reproductive and metabolic dysfunction. The underlying pathophysiology of PCOS primarily revolves around disturbance of the HPO (hypothalamic-pituitary-ovarian) axis. This dysregulation initiates with inadequate pulsatile secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus, resulting in sustained luteinizing hormone (LH) secretion. This unregulated secretion impairs the LH surge which is essential for ovulation [2].

The clinical manifestations of hyperandrogenism in individuals with PCOS may include hirsutism, which refers to excessive hair growth in areas such as the chin, abdomen, and upper thighs. Moreover, PCOS is also linked to obesity, infertility, and an increased risk of long-term cardiovascular diseases [3]. Given the diversity of symptoms associated with PCOS, adherence to standardized diagnostic criteria is of paramount importance in ensuring effective diagnosis and treatment. According to the Rotterdam Criteria, the diagnosis of PCOS necessitates the presence of at least two of the following three findings: (1) clinical or laboratory evidence of hyperandrogenism, (2) oligo-amenorrhea, and (3) polycystic ovarian morphology observed via ultrasonography [4]. Furthermore, the Androgen Excess Society (AES) Criteria emphasizes the importance of identifying hyperandrogenism and include the following requirements: (1) evidence of hyperandrogenism (either clinical signs such as hirsutism, acne, or alopecia, or biochemical evidence), (2) ovarian dysfunction (manifesting as oligo-amenorrhea, anovulation, or polycystic morphology), and (3) the exclusion of alternative disorders capable of producing similar symptoms, including congenital adrenal hyperplasia, androgen-secreting tumors, or Cushing's syndrome [5].

The prevalence of obesity among women with PCOS significantly exacerbates their risk of developing insulin resistance, which is a critical component of the syndrome [6]. Treatment options have evolved to include various pharmacological interventions, among which Metformin has emerged as a favorable alternative to sulfonylureas and insulin due to its weaker association with weight gain. Metformin is recognized for its potential to regulate blood glucose levels without increasing pancreatic insulin secretion. It achieves this goal by decreasing hepatic glucose production through mechanisms involving the alteration and inhibition of key hormonal pathways, particularly adenosine monophosphate kinase (AMPK) in gluconeogenesis, while also promoting glucose uptake by skeletal muscles [7]. In addition to its primary role in glycemic control, Metformin has demonstrated efficacy in alleviating other clinical manifestations of PCOS, including hirsutism, infertility, and menstrual irregularities [8].

Research in the field of PCOS has largely focused on enhancing awareness and understanding of its pathophysiology, diagnostic criteria, clinical characteristics, and treatment options.

Despite considerable research, there remains a notable gap in studies specifically evaluating the awareness levels among Saudi females concerning the significance of adherence to Metformin therapy in addressing insulin resistance and mitigating other manifestations of PCOS. This gap underscores the necessity of directing attention toward assessing both awareness and adherence to Metformin therapy, thereby delineating its vital role in the effective management of PCOS. The objective of this study was to evaluate the awareness of Saudi women concerning the indications for the use of Metformin in the context of managing PCOS.

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## **Materials and Methods**

#### Study design and type

A descriptive questionnaire-based cross-sectional study was conducted. The study was conducted over 2 months, November and December 2024.

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#### **Study population**

The study included women of reproductive age in Saudi Arabia (between menarche and menopause (15-49 years old). However, women who refused to participate, and those with cognitive impairments and/or a language barrier were excluded.

#### Sampling method

Convenience (non-random) sampling type, online chain referral. Copies of the electronic survey were distributed to our target population.

#### Sample size determination

To identify the target population, an extensive search of the General Authority for Statistics website was performed to determine the total number of targeted females. The estimated number of females in Saudi Arabia ranging from 15 - 49 years old is 4,990,995. The sample size calculation was performed via the WHO sample size calculation, which considers a 95% confidence interval, an absolute precision of 0.05%, and an anticipated population proportion of 50%. Based on these parameters, the minimum required sample size was determined to be 385.

#### **Data collection tools**

Data were collected via a self-administered online questionnaire distributed electronically via Google Forms, which are available in both Arabic and English for the targeted population. The questionnaire comprises several sections: a consent form, a sociodemographic data section, Section A, which focuses on the understanding of the long-term benefits of metformin use, and Section B, which addresses adherence to metformin therapy.

#### Statistical analysis plan

Version 22 of the Statistical Package for the Social Sciences (SPSS) program was used to analyze the data. The criteria of the analyzed sample were described using descriptive statistics in terms of means, standard deviations, medians, and interquartile ranges. The t-test was used to analyze the quantitative data, while the chi-square test was used to examine the association between the qualitative factors. Statistical significance was defined as a *P*-value of less than 0.05.

### Ethical part and confidentiality

The study protocol runs in compliance with the Helsinki Declaration and was approved by the biomedical research ethics committee of the Faculty of Medicine at the University.

Following ethical committee approval of the protocol, subjects gave their informed consent for participation in the study.

The objective of the research was clarified to each participant. Everyone had the choice of whether to take part or abstain. The participants were told that their comments would be confidential and would be used for research purposes only.

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## **Results**

Table 1 shows the demographic information for a sample of 436 participants. Most participants (90.6%) were Saudi, with a smaller proportion (9.4%) being non-Saudi. Most of the participants were from the North (46.6%), followed by the East (20.0%), Central (15.4%), West (14.4%), and South (3.7%).

Sample Description		F	%
Nationality	Saudi	395	90.6
	Non Saudi	41	9.4
Region	East	87	20.0
	West	63	14.4
	North	203	46.6
	South	16	3.7
	Central	67	15.4
Age group	Below 20	95	21.8
	20-30	169	38.8
	31-40	126	28.9
	41-50	43	9.9
	Above 50	3	0.7
Marital status	Single	221	50.7
	Married	201	46.1
	Divorced	12	2.8
	Widow	2	0.5
Educational level	High School or below	99	22.7
Educational level	Diploma	26	6.0
	Bachelor's degree	265	60.8
	Master's Degree	36	8.3
	PhD or higher	10	2.3
Employment status	Not working	180	41.3
	Working full time	79	18.1
	Working part-time	16	3.7
	Retired	1	0.2
	Student	160	36.7
Physical activity	Seldom	105	24.1
	Occasionally	245	56.2
	Often	86	19.7
Smoking	Non-smoker	393	90.1
	Current smoker	37	8.5
	Ex-smoker	6	1.4
Diagnosis status	I have been diagnosed with PCOS	144	33.0
	I have not been diagnosed with PCOS	292	67.0

**Table 1:** Demographic characteristics of the sample (N = 436).

The largest age group is 20-30 years (38.8%), followed by 31 - 40 years (28.9%), below 20 years (21.8%), 41 - 50 years (9.9%), and above 50 years (0.7%). Most participants were single (50.7%) or married (46.1%). A small percentage were divorced (2.8%) or widows (0.5%).

The majority of the participants had a Bachelor's degree (60.8%). Many participants were not working (41.3%), which could be attributed to students (36.7%) and participants who were retired or not actively seeking employment.

The majority of individuals engage in physical activity occasionally (56.2%). The majority of the participants 90.1%, were non-smokers. 67% of the participants were not diagnosed with PCOS.

Table 2 evaluates people's knowledge and comprehension (n = 436) about Polycystic Ovary Syndrome (PCOS) management. A majority of participants agreed (52.5%) that medications affecting male hormone production can help manage PCOS symptoms such as unwanted hair growth, acne, and alopecia. 57.6% of the participants agree that there is a general understanding that lowering insulin levels can be beneficial for PCOS management. Most participants (82.1%) are aware that insulin levels can be lowered through lifestyle changes like exercise and diet. 51.1% of the participants understood that medications can help lower insulin levels.

Knowledge about PCOS			%
Drugs that inhibit the effects of male hormones or prevent the ovary from producing	Agree	229	52.5
male hormones (such as hormonal contraception) might assist with alopecia, acne, and undesired hair growth.	Disagree	69	15.8
	I do not know	138	31.7
Reducing insulin levels may aid in weight loss, ovulation, and the reduction	Agree	251	57.6
of free testosterone.	Disagree	39	8.9
	I do not know	146	33.5
Exercise and some dietary adjustments can reduce insulin levels.	Agree	358	82.1
	Disagree	14	3.2
	I do not know	64	14.7
Drugs that increase the body's sensitivity to insulin can lower insulin levels.	Agree	223	51.1
	Disagree	59	13.5
	I do not know	154	35.3

**Table 2:** Assessment of knowledge regarding PCOS management (n = 436).

Table 3 assesses knowledge and perceptions about Metformin as a Polycystic Ovary Syndrome (PCOS) treatment. 36% have heard of metformin for PCOS treatment, and 47.9% have not. 16.1% are unsure. Effectiveness of Metformin for all Women with PCOS: 10.3% believe it's effective for all women. 70.9% are unsure if it is effective for all women. 18.8% believe it is not effective.

Awareness about Metformin		F	%
Have you heard of metformin being used as a treatment for PCOS before?	Yes	157	36.0
	No	209	47.9
	Not sure	70	16.1
Is Metformin effective for all women with PCOS?	Yes	45	10.3
	No	82	18.8
	Not sure	309	70.9

Do you think metformin is effective for	Yes	132	30.3
treating PCOS?	No	46	10.6
	Not sure	258	59.2
To the best of your knowledge, what	Reduces insulin levels	192	44.0
does metformin do for PCOS? (Multiple	Helps with weight loss	20	4.6
answers allowed)	Regulates menstrual cycles	143	32.8
	Assists with fertility	14	3.2
	I am not sure	67	15.4
Which of the following are recognized indications for using metformin in PCOS? (Select all that apply)	Managing insulin resistance	267	61.2
	Reducing symptoms of hyperandrogenism (e.g. excessive hair growth)	84	19.3
	Aiding in weight management	21	4.8
	Decreasing the risk of type 2 diabetes	14	3.2
	Menstrual Regulation	40	9.2
	Improving cholesterol levels	10	2.3
How did you first learn about metformin to treat PCOS?	Doctor/Healthcare provider	117	26.8
	Friends or family	37	8.5
	Media (TV, online, magazines)	43	9.9
	I have not heard of metformin before this survey	239	54.8

**Table 3:** Assessment of awareness regarding Metformin (n = 436).

**Effectiveness of metformin for treating PCOS:** 30.3% think metformin is effective for treating PCOS. 10.6% think it is not effective. 59.2% are unsure. In terms of the effect of Metformin: 44% believe it reduces insulin levels. 4.6% believe it helps with weight loss. 32.8% believe that it regulates menstrual cycles. 3.2% believe it assists with fertility. 15.4% are unsure.

**Recognized indications for metformin use in PCOS:** 61.2% recognize managing insulin resistance as an indication. 19.3% recognized reducing symptoms of hyperandrogenism as an indication. 4.8% recognized assisting in weight management as an indication. 3.2% recognized a decreased risk of type 2 diabetes as an indication. 9.2% recognize menstrual regulation as an indication. 2.3% recognize improving cholesterol levels as an indication.

**Source of information about metformin:** 26.8% learned about metformin from a doctor or healthcare provider. 8.5% learned from friends or family. 9.9% learned from media (TV, online, magazines). 54.8% had not heard of metformin before the survey.

Awareness of metformin for PCOS treatment is moderate, with a significant portion unaware. There is uncertainty about metformin's effectiveness for all women with PCOS and for treating PCOS in general. Understanding metformin's actions is primarily focused on insulin reduction and menstrual regulation. Managing insulin resistance is the most recognized indication for metformin use. Healthcare providers are the primary source of information about the use of metformin for treating PCOS.

Table 4 shows the perception and understanding of the long-term benefits of metformin in women with Polycystic Ovary Syndrome (PCOS). The table shows how participants rated various statements about the long-term effects of metformin use in PCOS. The participants were given the options to strongly agree, be neutral, disagree, strongly disagree, or indicate that they did not know. Metformin and Type 2 Diabetes: A significant majority (49.7%) strongly agrees or agrees that metformin helps lower the chance that women with PCOS will acquire type 2 diabetes. Only small percentages disagree or strongly disagree.

<b>Understanding of Long-term Benefits</b>		F	%
Metformin helps in reducing the risk of developing type 2 diabetes in	Strongly agree	100	22.9
women with PCOS.	Agree	117	26.8
	Neutral	121	27.8
	Disagree	21	4.8
	Strongly disagree	2	0.5
	I don't know	70	16.1
Continuous use of metformin can help in maintaining regular menstrual	Strongly agree	68	15.6
cycles over time in women with PCOS.	Agree	125	28.7
	Neutral	132	30.3
	Disagree	32	7.3
	Strongly disagree	4	0.9
	I don't know	70	16.1
Long-term use of metformin may improve fertility outcomes for women	Strongly agree	60	13.8
with PCOS.	Agree	98	22.5
	Neutral	151	34.6
	Disagree	44	10.1
	Strongly disagree	3	0.7
	I don't know	75	17.2
Using metformin over a long period can decrease the symptoms of	Strongly agree  Agree	61	14.0
hyperandrogenism (e.g. excessive hair growth, acne) in PCOS.		103	23.6
	Agree Neutral		34.6
	Disagree	37	8.5
	Strongly disagree	2	0.5
	I don't know	76	17.4
Metformin has a positive effect on weight management in the long term	Strongly agree	94	21.6
for women with PCOS.	Agree	120	27.5
	Neutral	126	28.9
	Disagree	25	5.7
	Strongly disagree	3	0.7
	I don't know	63	14.4

**Table 4:** Assessment of understanding of long-term benefits (n = 436).

**Metformin and menstrual cycles:** 44.3% strongly agreed or agreed that continuous metformin use helps maintain regular menstrual cycles over time in women with PCOS. A considerable number (30.3%) are neutral about this statement. Metformin and Fertility: While a significant portion, (36.3%) strongly agree or agree that long-term metformin use may improve fertility outcomes, 34.6% is neutral about this. Smaller percentages disagree or strongly disagree.

**Metformin and hyperandrogenism:** The majority (37.6%) strongly agree or agree that using metformin over a long period can decrease symptoms of hyperandrogenism (e.g. excessive hair growth, acne) in patients with PCOS. Significant portions (34.8%) are neutral about this statement.

**Metformin and weight management:** Metformin's effect on weight management concluded that 49.1% strongly agree or agree that metformin has a positive effect on weight management in the long term, and 28.9% are neutral. The table indicates a positive perception of metformin's long-term benefits in PCOS management.

Table 5 presents how individuals used metformin for the treatment of polycystic ovary syndrome (PCOS) and their adherence to the medication. Usage of Metformin: 65 patients (14.9%) used metformin for PCOS. Three hundred seventy-one patients (85.1%) do not use metformin for PCOS. Frequency of metformin usage: 22 patients (5.0%) took metformin as prescribed. Thirty-four patients (7.8%) take metformin most of the time. Three patients (0.7%) sometimes took metformin. Six patients (1.4%) rarely took metformin.

Adherence to Metformin Therapy		F	%
Do you use metformin to treat polycystic ovary	Yes	65	14.9
syndrome?	No	371	85.1
How often do you take your metformin medica-	Always	22	5.0
tion as prescribed?	Most of the time	34	7.8
	Sometimes	3	0.7
	Rarely	6	1.4
What are the main reasons you might miss a	Forgetfulness	25	5.7
dose of metformin?	Side effects	22	5.0
	I feel better without it	6	1.4
	I don't believe it is effective	5	1.1
	Financial reasons	2	0.5
	Other	5	1.1
How do you remember to take your metformin	Set reminders (e.g., alarm, mobile app)	20	4.6
medication?	Have a routine time for taking it	26	6.0
	Family/friends remind me	18	4.1
	Other	1	0.2
In the last six months, how often have you	More than once a month	6	1.4
discussed your metformin treatment with a healthcare provider?	Every 2-3 months	10	2.3
	Every 4-6 months	7	1.6
	Less than once every 6 months	16	3.7
	Never	26	6.0
If you have stopped taking metformin at any	Side effects	20	4.6
point, what were the reasons?	Did not see any improvement	9	2.1
	Advised by a doctor	6	1.4
	Switched to another treatment	7	1.6
	Financial reasons	5	1.1
	Did not stop taking it	15	3.4
	Other	3	0.7

**Table 5:** Assessment of adherence to metform in therapy (n = 436).

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**Reasons for missing metformin doses:** 25 patients (5.7%) missed doses due to forgetfulness. Twenty-two patients (5.0%) missed doses due to side effects. Six patients (1.4%) missed doses because they felt better without the medication. Five patients (1.1%) missed doses because they did not believe metformin was effective. 2 patients (0.5%) missed doses due to financial reasons. Five patients (1.1%) missed doses for other reasons.

**Reminders for taking metformin:** 20 patients (4.6%) use reminders to take metformin. 26 patients (6.0%) have a routine time for taking metformin. Eighteen patients (4.1%) relied on family/friends for reminders. 1 patient (0.2%) used other methods for reminders.

**Discussion with healthcare provider:** 6 patients (1.4%) discussed metformin treatment more than once a month. Ten patients (2.3%) discussed metformin treatment every 2-3 months. Seven patients (1.6%) discussed metformin treatment every 4-6 months. Sixteen patients (3.7%) discussed metformin treatment less than once every six months, and 26 patients (6.0%) have never discussed metformin treatment. Twenty patients (4.6%) stopped metformin due to side effects. Nine patients (2.1%) stopped metformin because they did not see any improvement. Six patients (1.4%) stopped metformin on the advice of a doctor. Seven patients (1.6%) stopped metformin to switch to another treatment. 5 patients (1.1%) stopped metformin due to financial reasons. Fifteen patients (3.4%) did not stop taking metformin. Three patients (0.7%) stopped metformin for other reasons.

#### **Discussion**

This research aimed to evaluate the awareness level of Saudi women regarding the indications for using metformin in the treatment of Polycystic Ovary Syndrome (PCOS). The findings reveal a moderate level of awareness regarding metformin treatment for PCOS, indicating a considerable gap in knowledge that requires attention.

A total of 61.2% of the respondents successfully identified managing insulin resistance as a primary indication for the use of metformin, suggesting a reasonable level of understanding among participants in this specific aspect. In contrast, awareness of other critical indications for metformin usage demonstrated significant shortcomings. Only 19.3% recognized its role in alleviating symptoms of hyperandrogenism, 9.2% acknowledged its potential to regulate menstrual cycles, 4.8% understood its use in assisting with weight management, 3.2% identified its benefit in lowering the chance of getting type 2 diabetes, and a mere 2.3% were aware of its ability to improve cholesterol levels.

These results align with prior research conducted by Aljuaid., *et al.* (2023), which similarly identified varying levels of awareness among participants concerning treatment options for PCOS, including metformin. In their study, an awareness rate of 64.9% (N = 246) was reported, illustrating a comparable trend in awareness [9]. Furthermore, research published by AlSinan., *et al.* (2017) indicated that 71.4% of participants demonstrated a lack of understanding regarding the pharmacological management of PCOS through metformin, particularly in controlling hyperinsulinemia [10].

A recent national study reported that a significant proportion of participants (n = 309, 74.8%) exhibited a good level of awareness concerning PCOS, whereas 104 individuals (25.2%) displayed a poor understanding of the condition. This awareness level was found to be significantly correlated with participants' educational attainment and marital status [11].

In a similar vein, a study conducted in Gurgaon, Haryana, India, aimed to assess the level of awareness surrounding PCOS among female college students. Using a structured questionnaire that addressed issues related to PCOS, menstrual cycles, and sociodemographic factors, this study included 428 participants with an average age of  $19.9 \pm 1.7$  years. The results indicated a troubling lack of awareness regarding PCOS among college-aged females [12].

In a broader context, the examination of awareness levels regarding treatment options for PCOS is not confined to Saudi Arabia. A parallel study conducted in Quetta, Pakistan, shed light on the awareness surrounding PCOS management strategies among participants.

The findings revealed a considerable lack of knowledge, with 25.7% of participants (116 individuals) unaware that symptomatic treatment options exist for managing PCOS. Additionally, 19.3% of the cohort (87 participants) did not recognize that antidiabetic medications, including metformin, apply to the treatment of this condition [13].

Similar trends were observed in a related study conducted in Klang Valley, Malaysia, which aimed to assess awareness of PCOS treatment among women in the region. A cross-sectional study found that a striking 71.7% of participants (294 individuals) lacked knowledge of the role of anti-diabetic medications, particularly metformin, in managing PCOS [14]. This considerable percentage reflects a widespread deficiency in understanding the full range of treatment options available for this condition.

The awareness level highlighted by this study underscores a critical need for improved public health interventions aimed at increasing knowledge surrounding PCOS treatment. The moderate awareness identified emphasizes the necessity for additional research and education to fill this vital gap in understanding.

## **Limitations of the Study**

This study on the awareness of Saudi women about the use of metformin for PCOS has some important limitations that should be taken into account. First, the data were collected solely through an online, web-based questionnaire distributed via social media. This method of data collection relies on the motivation and internet access of participants, which may have excluded women with PCOS symptoms who were unable to access or complete the survey.

Additionally, the participants were recruited independently based on their existing interest, awareness, or familiarity with PCOS. This self-selection process likely resulted in a sample that was more knowledgeable about the condition and its treatments compared to the broader population of Saudi women with PCOS. Women who were already informed about metformin's indications for PCOS may have been more inclined to participate in the study.

Furthermore, the use of an online survey carries the risk of non-response bias, where the characteristics of those who responded may differ in meaningful ways from those who did not participate. This could limit the generalizability of the findings to the overall population of Saudi women with PCOS.

In summary, the sampling approach and data collection method used in this research introduce several limitations that should be considered when interpreting the findings concerning Saudi women's awareness of the indications for using metformin in PCOS treatment. The self-selected and online-based nature of participant recruitment and data gathering may have influenced the results in ways that should be acknowledged.

## Conclusion

In conclusion, the majority of women had limited knowledge and understanding of this treatment. While most women with PCOS are aware of metformin as a medication, they lack detailed information about its specific indications and benefits for managing PCOS. Many women did not know that metformin can help regulate menstrual cycles, improve insulin resistance, and potentially assist with weight management - which are key treatment goals for PCOS.

This study highlights the need for enhanced education and awareness campaigns focused on Saudi women with polycystic ovary syndrome (PCOS). These efforts should aim to ensure a more comprehensive patient understanding of metformin and its role in managing this condition. Improving knowledge about the benefits of metformin, such as regulating menstrual cycles and improving insulin resistance, could increase the adoption of and adherence to this important PCOS therapy. Greater awareness among Saudi PCOS patients

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may lead to greater utilization of metformin as part of their disease management. Overall, the research underscores the necessity for more robust educational outreach to equip this population with stronger knowledge about metformin's therapeutic applications for PCOS.

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## **Declaration of Conflicting Interest**

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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