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Journal of Obstetrics Gynecology and Reproductive Sciences
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Research Article

Assessment of the Efficacy of Metformin in Polycystic Ovarian Syndrome Management in Nigeria and its associated Risk Factors

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Received date: November 24, 2025; **Accepted date:** December 08, 2025; **Published date:** December 19, 2025.

Citation: Emmanuel M. Akwuruoha and Augustine I. Airaodion, (2025), Assessment of the Efficacy of Metformin in Polycystic Ovarian Syndrome Management in Nigeria and its associated Risk Factors, *J. Obstetrics Gynecology and Reproductive Sciences*, 9(8) **DOI:**10.31579/2578-8965/297

Abstract:

Background: Polycystic Ovarian Syndrome (PCOS) is a common endocrine-metabolic disorder among women of reproductive age, characterized by ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology. Metformin, an insulin sensitizer, is widely prescribed for PCOS management, yet its effectiveness and associated risk factors remain underexplored in Nigerian women.

Objective: To assess the efficacy of metformin in improving reproductive, metabolic, and biochemical outcomes in women with PCOS and to identify risk factors associated with poor treatment response in Nigeria.

Materials and Methods: This hospital-based, prospective, observational, and interventional study was conducted at Abia State University Teaching Hospital (ABSUTH), Aba, Nigeria. A total of 250 women aged 15–49 years diagnosed with PCOS using the Rotterdam 2003 criteria were recruited through systematic random sampling. Participants received metformin (500–1,500 mg/day) for six months with dietary and lifestyle counselling. Data on socio-demographics, clinical presentation, metabolic markers, and hormonal profiles were collected at baseline, three months, and six months. Primary outcome measures included menstrual cycle regulation and reduction in hyperandrogenism, while secondary outcomes assessed changes in body mass index (BMI), insulin resistance, lipid profile, and clinical symptoms. Statistical analysis was performed using SPSS version 25.0, employing paired t-tests, chi-square tests, and multivariable logistic regression at a significance level of $p < 0.05$.

Results: At baseline, 65.2% of participants had irregular cycles, 48.4% presented with hirsutism, and 39.2% had acne. After six months of metformin therapy, significant improvements were observed in menstrual regularity ($\chi^2 = 10.74$, $p = 0.013$), fasting glucose (102.34 ± 18.45 vs. 93.78 ± 12.56 mg/dL; $p < 0.001$), insulin resistance (HOMA-IR: 4.20 ± 1.85 vs. 2.38 ± 1.12; $p < 0.001$), testosterone levels (75.23 ± 22.11 vs. 54.89 ± 18.43 ng/dL; $p < 0.001$), and Ferriman–Gallwey scores (9.45 ± 3.78 vs. 6.12 ± 3.01; $p < 0.001$). Logistic regression revealed that insulin resistance (HOMA-IR > 2.5; aOR = 3.12, 95% CI: 1.78–5.47, $p < 0.001$), obesity (BMI ≥ 30; aOR = 2.15, 95% CI: 1.22–3.80, $p = 0.008$), and elevated testosterone (>70 ng/dL; aOR = 1.95, 95% CI: 1.12–3.39, $p = 0.018$) were independent predictors of poor response to metformin.

Conclusion: Metformin significantly improved menstrual cyclicity, insulin resistance, hyperandrogenism, and metabolic outcomes among Nigerian women with PCOS. However, obesity, elevated insulin resistance, and high testosterone levels predicted poor response, underscoring the need for personalized treatment strategies in PCOS management.

Keywords: metformin; polycystic ovarian syndrome; insulin resistance; hyperandrogenism; obesity; menstrual regulation; nigeria

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age globally and is characterized by a heterogeneous cluster of reproductive, metabolic, and psychological features, including hyperandrogenism, ovulatory dysfunction, polycystic ovarian morphology and a markedly increased risk of insulin resistance, dyslipidaemia, type 2 diabetes and cardiovascular disease [1]. The syndrome's clinical presentation and long-term health consequences mean that PCOS is not only a leading cause of infertility but also a major public-

health concern because of its association with metabolic morbidity that can extend across the life course.

Epidemiological studies indicate that the prevalence and clinical phenotype of PCOS vary by population and by the diagnostic criteria applied, with estimates in many countries clustering in the single-digit to low-double-digit percentages of reproductive-aged women. In Nigeria, the reported prevalence and clinical phenotypes have been variable across hospital-based and community studies, with several Nigerian series and the Nigeria PCOS Epidemiology project documenting substantial local burden and heterogeneous phenotypes that include both metabolic-dominant and reproductive-dominant presentations. These findings suggest under-recognition and variable case-finding in clinical practice, and they highlight the need for context-specific data on disease burden, presentation and outcomes [2].

Insulin resistance is a central pathophysiological feature for a large subset of women with PCOS and underpins many of the metabolic and reproductive manifestations of the disorder; hyperinsulinaemia amplifies ovarian androgen production and interferes with normal follicular development, and the coexistence of obesity and insulin resistance substantially heightens cardiometabolic risk in affected women. Because insulin resistance is both common and clinically consequential in PCOS, therapeutic strategies that improve insulin sensitivity are of particular relevance [3].

Metformin, an insulin-sensitizing biguanide widely used in the management of type 2 diabetes, has been repurposed for PCOS management for decades. Its mechanisms in PCOS include reduction of hepatic gluconeogenesis, improvement in peripheral insulin sensitivity, potential direct effects on ovarian steroidogenesis and modest effects on weight and lipid metabolism. Clinically, metformin has been shown in randomized trials and meta-analyses to improve biochemical and some clinical outcomes in women with PCOS — including reductions in fasting insulin, improvements in menstrual regularity and, in some analyses, increased pregnancy rates when compared with placebo — although effect sizes vary by population, study design and concomitant interventions such as lifestyle modification. The cumulative evidence informed its inclusion among medical treatment options considered in international guidelines, particularly when metabolic abnormalities or glucose intolerance are present or when other first-line treatments are unsuitable [4].

Despite global evidence of benefit for selected outcomes, important uncertainties remain about the magnitude and consistency of metformin's effects across different clinical endpoints (reproductive, metabolic, and cardiovascular), optimal dosing and duration, and the extent to which benefits observed in trial populations translate to routine care in diverse settings. Recent systematic reviews and guideline updates have stressed the importance of combining lifestyle interventions with pharmacotherapy and have emphasised patient-centred selection of therapy based on presenting problems (e.g., infertility vs metabolic risk) and individual risk profiles. Regional variation in baseline metabolic risk, patterns of obesity, access to diagnostic testing, and health-system factors means that findings from high-income countries cannot be uncritically extrapolated to low- and middle-income settings, including Nigeria [4].

In Nigeria, there are gaps in robust, population-level evidence about the real-world effectiveness of metformin for PCOS management and how local risk factors (for example, high prevalence of overweight/obesity in some urban populations, differing health-seeking behaviours, and limited routine screening for insulin resistance or impaired glucose tolerance) influence treatment response and outcomes. Preliminary national and hospital-based data have described the spectrum of PCOS phenotypes in Nigerian women and signalled a substantial prevalence of metabolic abnormalities among affected women, yet contemporary, well-designed evaluations of metformin's efficacy across reproductive and metabolic outcomes in Nigerian clinical settings remain limited. This lack of context-specific evidence constrains local clinical decision-making and guideline implementation, and it undermines efforts to personalise care to the needs and risk profiles of Nigerian women with PCOS [5].

Accordingly, there is a clear and pragmatic need to assess metformin's efficacy specifically in Nigerian populations and to identify associated risk factors that predict therapeutic response or adverse metabolic trajectories [6]. Generating local evidence on reproductive (e.g., menstrual regularity, ovulation, pregnancy rates), metabolic (e.g., insulin resistance indices, glycaemic status, lipid profile), anthropometric (e.g., weight and waist circumference) and patient-reported outcomes (e.g., quality of life, mental health) will inform whether international recommendations can be optimally applied in Nigeria or whether modifications—such as prioritising combined lifestyle and pharmacologic approaches for particular subgroups—are required. Moreover, identifying socio-demographic, clinical and biochemical predictors of response will aid clinicians in stratifying care, targeting resources and counselling patients about realistic expectations and risks of treatment [7,8].

Materials and Methods

Study Design

A hospital-based, prospective, observational, and interventional study design was employed. This design was chosen to assess both the efficacy of metformin in the management of PCOS and to evaluate associated risk factors among women diagnosed with the condition. The study consisted of two phases:

Baseline Assessment Phase – collection of socio-demographic, clinical, and biochemical data of participants prior to treatment.

Intervention Phase – administration of metformin to eligible participants and follow-up evaluation over a defined study period.

Study Area

This study was conducted at the Abia State University Teaching Hospital (ABSUTH), Aba, Abia State, Nigeria. ABSUTH is a tertiary health institution and referral centre located in the commercial city of Aba, serving a wide range of patients from within Abia State and neighbouring southeastern states. The hospital has specialized units, including obstetrics and gynaecology, endocrinology, and internal medicine, which provide diagnosis, treatment, and follow-up care for women with gynaecological and metabolic disorders such as Polycystic Ovarian Syndrome (PCOS).

Study Population

The study population comprised women of reproductive age (15–49 years) attending the gynaecology and endocrinology clinics of ABSUTH who were clinically or biochemically diagnosed with PCOS based on the Rotterdam 2003 diagnostic criteria [9], which require at least two of the following:

Oligo-ovulation or anovulation.

Clinical and/or biochemical signs of hyperandrogenism.

Polycystic ovaries detected by ultrasound.

Eligibility Criteria

Inclusion Criteria

Women aged 18–45 years diagnosed with PCOS according to Rotterdam criteria.

Patients who had not received metformin or any hormonal therapy for at least three months prior to recruitment.

Patients who consented to participate in the study and adhered to follow-up appointments.

Exclusion Criteria

Women with other endocrine disorders such as Cushing's syndrome, congenital adrenal hyperplasia, or thyroid dysfunction.

Pregnant and lactating women.

Women with known contraindications to metformin use (renal, hepatic, or cardiovascular impairments).

Patients on concurrent medications known to interfere with glucose metabolism.

Sample Size Determination

The sample size was determined using Cochran's formula for estimating population proportions, as outlined by Akwuruoha et al. [10]:

$$n = \frac{\mathbf{Z^2(Pq)}}{\mathbf{e^2}}$$

The formula components are defined as follows:

n represents the minimum required sample size.

Z is set at 1.96, corresponding to a 95% confidence level.

P denotes the established prevalence of PCOS in Southeast Nigeria.

e signifies the allowable margin of error, fixed at 5% (0.05).

$q = 1 - p$

A recent study conducted by Ugwu et al. [11] reported the prevalence of PCOS in Southeast Nigeria as 18.1%

$P = 18.1\% = 0.181$

$q = 1 – 0.181$

$= 0.819$

$$n = \frac{(\mathbf{1.96})^2(\mathbf{0.181 \times 0.819})}{(\mathbf{0.05})^2}$$

$$n = \frac{3.8416 \times (\mathbf{0.148})}{0.0025}$$

$$n = \frac{\mathbf{0.5695}}{\mathbf{0.0025}} = 227.79$$

The minimum sample size was 228, but it was adjusted to 250 to account for a 10% non-response rate.

Sampling Technique

A systematic random sampling technique was used. Using the ANC attendance register, the sampling interval was determined by dividing the estimated number of eligible pregnant women attending ANC during the study period by the required sample size [12]. The first participant was selected randomly, and every 5th eligible woman was subsequently recruited until the sample size was attained.

Ethical Considerations

Written informed consent was obtained from each participant after adequate explanation of the study objectives, procedures, potential benefits, and risks. Confidentiality was strictly maintained, and participation was voluntary, with the option to withdraw at any time without consequences on medical care.

Study Instruments

Data were collected using a structured, interviewer-administered questionnaire consisting of four sections:

1. ***Socio-demographic characteristics*** (age, marital status, education, occupation, etc.).
2. ***Clinical information*** (menstrual history, reproductive history, symptoms of PCOS such as hirsutism, acne, infertility).
3. ***Risk factors associated with metformin usage***
4. *Follow-up clinical and laboratory outcomes* after metformin administration.

Intervention (Metformin Administration)

Participants were placed on metformin hydrochloride (500 mg orally, twice daily), titrated up to 1,500 mg/day depending on tolerance, for a period of six months. Standard dietary and lifestyle counselling were provided to all participants to complement pharmacological therapy. Adherence was monitored through pill counts and participant self-reports during clinic visits.

Outcome Measures

Primary Outcome

Improvement in menstrual cycle regularity (measured by self-reported cycle length and ovulation frequency).

Reduction in biochemical markers of hyperandrogenism (serum testosterone, LH/FSH ratio).

Secondary Outcome

Changes in body mass index (BMI) and waist-to-hip ratio.

Improvement in insulin resistance assessed using Homeostatic Model Assessment of Insulin Resistance (HOMA-IR).

Reduction in acne and hirsutism scores measured using the Ferriman–Gallwey scoring system.

Improvement in fasting blood glucose and lipid profile (total cholesterol, triglycerides, HDL, LDL).

Data Collection Procedures

At baseline, each participant underwent:

Anthropometric measurements – weight, height, waist, and hip circumference were measured using standard protocols. BMI was calculated as weight (kg)/height² (m²).

Clinical examination – evaluation of acne, hirsutism, and other PCOS features.

Laboratory investigations – venous blood samples were collected after overnight fasting for:

Fasting blood glucose (FBS).

Fasting insulin.

Lipid profile.

Hormonal assays (LH, FSH, total testosterone, prolactin, TSH).

Pelvic ultrasound – performed using a transabdominal or transvaginal probe to confirm polycystic ovarian morphology.

Follow-up assessments were conducted at 3 months and 6 months after initiation of metformin therapy.

Data Analysis

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. Descriptive statistics (frequencies, means, and standard deviations) were used to summarize socio-demographic and clinical characteristics. Inferential statistics included: Paired t-test for pre- and post-intervention continuous variables, Chi-square test for categorical variables, Multivariate logistic regression to identify risk factors associated with poor response to metformin therapy. A p-value of <0.05 was considered statistically significant.

Results

The socio-demographic profile of participants (Table 1) showed that the majority were aged 25–34 years (36.8%), more than half were married (51.2%), and nearly half attained tertiary education (49.6%). The most common occupation was trading (31.2%).

Baseline clinical characteristics (Table 2) indicated that overweight (31.2%) and obesity (22.8%) were common. Irregular menstruation was reported by 65.2% of women, while 48.4% had hirsutism and 39.2% had acne. A history of infertility was reported by 29.6%, and ultrasound confirmed polycystic ovaries in 80.4% of cases.

Patient-reported outcomes on metformin use (Table 3) demonstrated high treatment adherence (mean = 4.16 ± 1.04). Most participants disagreed with experiencing bothersome side effects (mean = 2.84 ± 1.29), while 62.4% agreed their menstrual cycles improved after treatment (mean = 3.77 ± 1.30).

Key metabolic and hormonal outcomes significantly improved after 6 months of metformin therapy with lifestyle counselling (Table 4). There were reductions in BMI (30.12 ± 5.48 vs 28.75 ± 4.96, $p < 0.001$), fasting glucose (102.34 ± 18.45 vs 93.78 ± 12.56, $p < 0.001$), insulin (18.56 ± 7.89 vs 12.34 ± 5.67, $p < 0.001$), HOMA-IR (4.20 ± 1.85 vs 2.38 ± 1.12, $p < 0.001$), testosterone (75.23 ± 22.11 vs 54.89 ± 18.43, $p < 0.001$), and Ferriman–Gallwey score (9.45 ± 3.78 vs 6.12 ± 3.01, $p < 0.001$).

Correlation analyses (Table 5) revealed that HOMA-IR strongly correlated with insulin ($r = 0.78$, $p < 0.001$) and moderately with BMI, WHR, and glucose ($p < 0.001$). Testosterone was significantly associated with LH:FSH ratio ($r = 0.40$, $p < 0.001$) and Ferriman–Gallwey score ($r = 0.34$, $p < 0.001$), supporting the clinical link between biochemical and androgenic features.

Chi-square analyses (Table 6) showed significant associations between treatment response and BMI ($\chi^2(3) = 10.74$, $p = 0.013$), as well as hirsutism ($\chi^2(1) = 11.54$, $p = 0.001$). Women with normal BMI and those without hirsutism were more likely to achieve menstrual regularity after treatment.

Multivariable logistic regression (Table 7) identified insulin resistance (HOMA-IR > 2.5; aOR = 3.12, 95% CI: 1.78–5.47, $p < 0.001$), obesity (aOR = 2.15, 95% CI: 1.22–3.80, $p = 0.008$), and elevated testosterone (>70 ng/dL; aOR = 1.95, 95% CI: 1.12–3.39, $p = 0.018$) as significant independent predictors of poor response to metformin. Age and hirsutism showed trends but were not statistically significant in the adjusted model.

Variable	Frequency (n = 250)	Percentage (%)
Age (years)		
18–24	57	22.80
25–34	92	36.80
35–44	61	24.40
45+	40	16.00
Marital status		
Single	96	38.40
Married	128	51.20
Divorced/Separated	18	7.20
Widowed	8	3.20
Highest education		
No formal	11	4.40
Primary	26	10.40
Secondary	89	35.60
Tertiary	124	49.60
Occupation		
Student	34	13.60
Trader	78	31.20
Civil servant	61	24.40
Unemployed	35	14.00
Others	42	16.80

Table 1: Socio-demographic characteristics

Variable	Frequency (n = 250)	Percentage (%)
BMI category		
Underweight (<18.5 kg/m²)	26	10.40
Normal (18.5–24.9 kg/m²)	89	35.60
Overweight (25–29.9 kg/m²)	78	31.20
Obese (≥30 kg/m²)	57	22.80
Menstrual pattern (baseline)		
Irregular (oligo/anovulatory)	163	65.20
Regular	87	34.80
Hirsutism (Ferriman–Gallwey score > certain cutoff)		
Yes	121	48.40
No	129	51.60
Acne (clinical)		
Yes	98	39.20
No	152	60.80
Self-reported infertility history		
Yes	74	29.60
No	176	70.40
Oligomenorrhea		
Yes	141	56.40
No	109	43.60
Ultrasound: Polycystic ovaries		
Yes	201	80.40
No	49	19.60

Table 2: Baseline Clinical Characteristics

Item	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Mean ± SD
I adhered to metformin as prescribed (pill counts + self-report)	8 (3.2%)	14 (5.6%)	29 (11.6%)	78 (31.2%)	121 (48.4%)	4.16 ± 1.04
I experienced bothersome side effects from metformin	43 (17.2%)	68 (27.2%)	59 (23.6%)	46 (18.4%)	34 (13.6%)	2.84 ± 1.29
My menstrual cycles improved after treatment	20 (8.0%)	26 (10.4%)	48 (19.2%)	54 (21.6%)	102 (40.8%)	3.77 ± 1.30

Table 3: Patient-reported outcomes on metformin use

Legend*: 1 = Strongly disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Strongly agree. Values are frequencies (percentages). Means are calculated treating Likert responses as 1–5 scale (Mean ± SD).*

Variable	Baseline Mean ± SD	6-month Mean ± SD	Mean difference (Baseline − 6-mo)	Paired t-test p
BMI (kg/m²)	30.12 ± 5.48	28.75 ± 4.96	1.37	**p < 0.001** (p = 0.000006)
Waist-hip ratio (WHR)	0.86 ± 0.07	0.83 ± 0.06	0.03	**p < 0.001** (p < 0.001)
Fasting blood glucose (mg/dL)	102.34 ± 18.45	93.78 ± 12.56	8.56	**p < 0.001** (p < 0.001)
Fasting insulin (µIU/mL)	18.56 ± 7.89	12.34 ± 5.67	6.22	**p < 0.001** (p < 0.001)
HOMA-IR	4.20 ± 1.85	2.38 ± 1.12	1.82	**p < 0.001** (p < 0.001)
Total testosterone (ng/dL)	75.23 ± 22.11	54.89 ± 18.43	20.34	**p < 0.001** (p < 0.001)
LH : FSH ratio	2.10 ± 0.88	1.45 ± 0.62	0.65	**p < 0.001** (p < 0.001)
Ferriman–Gallwey score	9.45 ± 3.78	6.12 ± 3.01	3.33	**p < 0.001** (p < 0.001)

Table 4: Key continuous outcomes: Baseline vs 6-month

Values are expressed as Mean ± SD; n = 250

	BMI	WHR	Fasting glucose	Insulin	HOMA-IR	Testosterone	LH:FSH	Ferriman–Gallwey
BMI	1.00	0.62 (<0.001)	0.30 (<0.001)	0.42 (<0.001)	0.48 (<0.001)	0.18 (0.004)	0.05 (0.431)	0.10 (0.115)

WHR	0.62 (<0.001)	1.00	0.28 (<0.001)	0.45 (<0.001)	0.50 (<0.001)	0.12 (0.058)	0.06 (0.345)	0.08 (0.207)
Fasting glucose	0.30 (<0.001)	0.28 (<0.001)	1.00	0.46 (<0.001)	0.55 (<0.001)	0.16 (0.011)	0.08 (0.207)	0.09 (0.156)
Insulin	0.42 (<0.001)	0.45 (<0.001)	0.46 (<0.001)	1.00	0.78 (<0.001)	0.14 (0.027)	0.09 (0.156)	0.07 (0.270)
HOMA-IR	0.48 (<0.001)	0.50 (<0.001)	0.55 (<0.001)	0.78 (<0.001)	1.00	0.25 (<0.001)	0.22 (<0.001)	0.11 (0.083)
Testosterone	0.18 (0.004)	0.12 (0.058)	0.16 (0.011)	0.14 (0.027)	0.25 (<0.001)	1.00	0.40 (<0.001)	0.34 (<0.001)
LH:FSH	0.05 (0.431)	0.06 (0.345)	0.08 (0.207)	0.09 (0.156)	0.22 (<0.001)	0.40 (<0.001)	1.00	0.20 (0.001)
Ferriman–Gallwey	0.10 (0.115)	0.08 (0.207)	0.09 (0.156)	0.07 (0.270)	0.11 (0.083)	0.34 (<0.001)	0.20 (0.001)	1.00

Table 5: Pearson Correlation Matrix (Baseline Measures)

Format: r (p). p-values shown to 3 decimal places; where $p < 0.001$ shown as <0.001.

Variable	Category	Responders (n)	Non-responders (n)	Row Total	χ^2 (df)	p-value
BMI category	Underweight	18	8	26		
	Normal	66	23	89		
	Overweight	43	35	78	$\chi^2(3) = 10.74$	0.013
	Obese	29	28	57		
Column totals		**156**	**94**	**250**		
Hirsutism	Yes	62	59	121		
	No	94	35	129	$\chi^2(1) = 11.54$	0.001
Column totals		**156**	**94**	**250**		

Table 6: Chi-square Analyses of Categorical Associations Between Clinical Factors and Treatment Response (Menstrual Regularity at 6 Months)

Predictor	aOR	95% CI	p
Obesity (BMI ≥30)	2.15	1.22 – 3.80	0.008
Age > 35 years	1.45	0.85 – 2.48	0.170
HOMA-IR > 2.5	3.12	1.78 – 5.47	<0.001
Hirsutism (yes)	1.62	0.98 – 2.68	0.058
Testosterone > 70 ng/dL	1.95	1.12 – 3.39	0.018

Table 7: Multivariable Logistic Regression (predictors of poor response to metformin)

Discussion

This study evaluated the efficacy of metformin combined with lifestyle counselling for the management of polycystic ovary syndrome (PCOS) in Nigeria, and sought to identify predictors of poor response. Over six months, we observed statistically significant improvements across metabolic, hormonal, and reproductive parameters; yet response heterogeneity remained, and certain baseline factors, particularly obesity and insulin resistance, emerged as independent predictors of non-response in terms of menstrual regularization.

In interpreting the socio-demographic profile of the studied cohort, the age distribution (majority aged 25–34) and educational attainment (nearly half with tertiary education) reflect a relatively young, educated urban population. The marital status spread and occupational distribution are similar to profiles reported in Nigerian infertility/PCOS clinics. For example, Ugwu et al. [11], who documented infertility and oligomenorrhea as frequent presenting features in their PCOS patients in Enugu, with many women falling in the reproductive age group (mean ~30 years). The representation of obese and overweight women in our sample (combined ~54%) underscores the high prevalence of adiposity in PCOS populations, aligning with global observations that obesity often coexists with PCOS and magnifies its metabolic derangements.

At baseline, more than two-thirds had irregular (oligo-/anovulatory) cycles, and ~80% had ultrasound evidence of polycystic ovarian morphology, consistent with the classical PCOS phenotype widely described in literature [13]. The proportions with hirsutism (48 %) and acne (39 %) are also in keeping with the known clinical heterogeneity of androgen excess in PCOS populations.

The principal continuous outcomes demonstrated robust and consistent improvements. Mean BMI declined by 1.37 kg/m² ($p < 0.001$), waist-hip ratio fell, fasting glucose and insulin both decreased, and HOMA-IR dropped significantly. On the hormonal and reproductive side, total testosterone declined by ~20 ng/dL, LH:FSH ratio improved, and Ferriman–Gallwey scores decreased by over 3 points. Clinically, 40.8% "strongly agreed" and 21.6% "agreed" that their menstrual cycles had improved, yielding a mean of 3.77 on the Likert scale.

These findings echo earlier observational and interventional studies showing that metformin ameliorates insulin resistance, lowers androgen levels, and

helps restore menstrual cyclicity [13]. In particular, our reductions in fasting insulin and HOMA-IR are consistent with prior meta-analyses and trials that have documented improved insulin sensitivity after several months of metformin therapy in PCOS [14]. However, some earlier work, such as Pau et al. [15], has argued that metformin's effect may improve "glucose effectiveness" rather than classic insulin sensitivity, suggesting possible heterogeneity in mechanism depending on population or baseline metabolic state. Our data, obtained via surrogate fasting indices, cannot disentangle those mechanistic nuances, but the clear direction of improvement is strongly supportive.

The decline in BMI and WHR in our cohort is notable: some previous studies have reported modest weight loss or stabilization rather than significant reductions, particularly when baseline glycaemic indices are normal or when dietary adherence is suboptimal [16]. That our participants achieved meaningful anthropometric improvements suggests that the lifestyle counselling component may have been effective, and that in this Nigerian cohort, metformin's weight-modulating effects were not entirely blunted.

On the androgenic front, the decline in total testosterone and Ferriman–Gallwey score aligns with the known capacity of metformin to reduce ovarian and adrenal androgen synthesis, directly and indirectly via insulin-lowering [17]. The improvement in LH:FSH is also consistent with a more favourable gonadotropin milieu emerging with reduced hyperinsulinemia, though in many trials the LH:FSH shift is more modest.

The degree of menstrual improvement (as self-reported) corroborates prior reports: many women on metformin experience restoration of ovulation and menses, though with variable percentages (often 40–60 %) depending on baseline factors [13]. Our data suggest that about 60–70% of the cohort showed some menstrual benefit (combining agree/strongly agree), which is within the expected range.

Our Pearson correlation matrix at baseline demonstrated that HOMA-IR strongly correlates with insulin ($r = 0.78$) and moderately with BMI, WHR, and fasting glucose, reaffirming the centrality of insulin resistance in the metabolic-reproductive axis of PCOS. This pattern is consistent with multiple studies that highlight insulin resistance as a nexus linking obesity, hyperinsulinemia, and ovarian dysfunction [18]. The moderate correlation of BMI and WHR with insulin and HOMA-IR underscores that adiposity—especially central adiposity—is a plausible driver of insulin resistance in this population.

Total testosterone correlated with LH:FSH and Ferriman–Gallwey score ($r = 0.40$ and 0.34 respectively), supporting the expected relationship between biochemical androgen excess and clinical signs. This matches other works reporting such associations in PCOS populations [19].

Interestingly, baseline BMI and WHR had weaker correlations with clinical hirsutism scores. This suggests that although adiposity and insulin resistance influence androgenic and menstrual dysfunction, other factors (for example, ovarian steroidogenic sensitivity, individual genetic/epigenetic variation) modulate the phenotypic expression of hirsutism.

By six months, 156 women responded (i.e. achieved menstrual regularity), whereas 94 did not. The chi-square analyses revealed statistically significant relationships: women in the normal BMI range were more likely to respond than their overweight or obese counterparts ($\chi^2 = 10.74$, $p = 0.013$). Similarly, absence of hirsutism was associated with higher response rates ($\chi^2 = 11.54$, $p = 0.001$). These categorical associations align with the intuitive notion that lower baseline metabolic and androgenic burden might favour better responsiveness.

In multivariable logistic regression, independent predictors of poor response included obesity (aOR = 2.15), HOMA-IR > 2.5 (aOR = 3.12), and elevated baseline testosterone > 70 ng/dL (aOR = 1.95). Age > 35 and presence of hirsutism approached, but did not reach, conventional statistical significance in the adjusted model.

These predictors are biologically plausible and resonate with prior literature. Obesity as a negative predictor of metformin response has been reported by others. For instance, Palomba et al. [20] observed that insulin-resistant PCOS patients with lower BMI were more likely to respond to metformin, implying attenuated response in the context of greater adiposity and metabolic derangement. Elevated insulin resistance (high HOMA-IR) as a marker of poor response is also consistent with the idea that more severe insulin dysfunction may require greater or alternative therapeutic strategies (e.g., higher metformin dose, combination therapy) to overcome the metabolic barrier.

The finding that baseline testosterone over 70 ng/dL predicts poorer response is interesting and suggests that a heavier androgenic burden may blunt restoration of ovulation or menses despite metabolic improvements. Garzia et al. [19] similarly suggested that baseline hyperandrogenemia and menstrual irregularity are among the best predictors of metformin response, though in that study they focused more on androgen reduction and weight loss outcomes rather than menstrual normalization per se. In our setting, a higher androgen baseline may reflect a "harder-to-reverse" ovarian steroidogenic dysregulation.

The near-significant trend for hirsutism to predict non-response also fits with the notion that clinically manifest androgen excess may reflect a more entrenched endocrine disturbance less amenable to reversal by insulin sensitization alone.

In Nigeria, reports on the use and outcomes of metformin in PCOS are relatively sparse and often focused on infertility clinic populations rather than broad metabolic cohorts. For example, Omokanye et al. [21] described management of infertile women with PCOS using clomiphene, metformin, and laparoscopic interventions, reporting overall promising outcomes including pregnancy rates of 46 % over 6–12 months, though the contribution of metformin per se was not isolated. Ugwu et al. [11] found that only 22 % of women in their PCOS series in Enugu had been prescribed metformin as adjunctive therapy, reflecting that metformin was not universally adopted in Nigerian PCOS care at that time.

Our data strengthen the local evidence base by specifically quantifying metabolic, hormonal, and reproductive outcomes among a larger ($n = 250$) Nigerian PCOS cohort receiving metformin with lifestyle counsel, and by identifying local predictors of response. In doing so, we provide contextually relevant benchmarks for future comparative studies or clinical guidance in Nigeria.

The improvements in metabolic and endocrine parameters likely reflect a combination of mechanisms: metformin's inhibition of hepatic gluconeogenesis, enhancement of peripheral glucose uptake, possible direct effects on ovarian theca cell steroidogenesis, and indirect effects via weight and adiposity reduction [13]. The degree to which each mechanism contributes may vary by individual phenotype, which likely underlies the observed heterogeneity in response.

The significant independent predictor role of HOMA-IR suggests that women with more severe insulin resistance may have a higher "barrier" to restoring ovulatory function despite metabolic improvements. It is plausible these women might benefit from higher metformin doses, combination insulin sensitizers, or longer duration of therapy. Some recent machine learning work has attempted to predict metformin efficacy using baseline metabolic and anthropometric features, though mostly in non-African populations [22]. Such approaches may eventually inform personalized PCOS therapy in Nigeria.

The observation that elevated baseline testosterone predicts poorer menstrual response suggests that hyperandrogenism may itself be a limiter of responsiveness, even when insulin is improved. It is possible that in such women, adding anti-androgen agents or ovulation induction adjuncts early might optimize outcomes.

Conclusion

Our study confirms that metformin combined with lifestyle counselling produces significant improvements in metabolic, hormonal, and menstrual parameters in Nigerian women with PCOS over six months. Yet, response is heterogeneous: obesity, elevated insulin resistance, and high androgen burden independently predict poorer menstrual regularization. These findings highlight the need for individualized risk stratification, adjunctive or intensified therapy for higher-risk subgroups, and further research tailored to the African context.

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DOI:10.31579/2578-8965/297