https://doi.org/10.48047/AFJBS.6.16.2024.4416-4424

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Assessing the Effects of Metformin on Lipid Metabolism in Women with Polycystic Ovarian Syndrome

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Received: 21 Sep, 2024
Accepted: 29 Nov, 2024
Published: 23 Dec, 2024
doi:10.48047/AFJBS.6.16.2024.4416-4424

ABSTRACT

Background

'Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age, often associated with metabolic disturbances, including insulin resistance and dyslipidemia'. Metformin, an insulin-sensitizing agent, is frequently used to manage metabolic dysfunction in PCOS, but its effects on lipid metabolism remain an area of interest. This study evaluates the 'impact of Metformin on lipid parameters in women with PCOS'.

Methods

A prospective interventional study was conducted at Jinnah Medical College, Peshawar, from January 2023 to January 2024. A total of 103 women diagnosed with PCOS based on the Rotterdam criteria were included. Participants received Metformin therapy for three months, and their metabolic parameters were assessed before and after treatment. Fasting blood glucose, fasting insulin, HOMA-IR, and lipid profile (total cholesterol, LDL-C, HDL-C, triglycerides, and VLDL) were measured using standard biochemical methods. Changes in lipid and metabolic parameters were analyzed using paired statistical tests.

Results

Following Metformin therapy, significant improvements were observed in lipid metabolism. LDL-C levels decreased from 132.6 mg/dL to 118.2 mg/dL ($p<0.001$), 'while total cholesterol dropped from 201.8 mg/dL to 184.5 mg/dL ($p<0.001$). HDL-C increased from 39.5 mg/dL to 44.8 mg/dL ($p<0.001$), and triglycerides were reduced from 172.4 mg/dL to 146.9 mg/dL ($p<0.001$)'. Additionally, fasting insulin levels and HOMA-IR showed significant reductions, indicating improved insulin sensitivity. There was also a notable improvement in menstrual cycle regularity and a reduction in hyperandrogenic symptoms.

Conclusion

Metformin therapy positively influences lipid metabolism, insulin resistance, and hormonal balance in women with PCOS. By lowering LDL-C and triglycerides while increasing HDL-C, Metformin contributes to a healthier lipid profile, potentially reducing long-term cardiovascular risks in this population. 'These findings support the role of Metformin as an effective metabolic therapy in PCOS management'. Further research is recommended to explore its long-term effects on cardiovascular outcomes.

Keywords

Polycystic ovary syndrome, Metformin, Lipid metabolism, Insulin resistance, Dyslipidemia, Cardiovascular risk, PCOS treatment

INTRODUCTION

'Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age' [1]. 'It is characterized by a combination of menstrual irregularities, hyperandrogenism, and polycystic ovarian morphology'. 'The condition is also associated with metabolic disturbances, including insulin resistance, obesity, and dyslipidemia, which increase the risk of developing type 2 diabetes and cardiovascular diseases' [2]. Due to its complex and multifactorial nature, managing PCOS requires a comprehensive approach that targets both reproductive and metabolic abnormalities[3].

Among the various treatment options, Metformin has emerged as a widely used medication for managing metabolic dysfunction in PCOS. 'Originally developed as an antihyperglycemic agent for type 2 diabetes, Metformin improves insulin sensitivity, reduces hepatic glucose production, and enhances peripheral glucose uptake' [4]. 'Beyond its effects on glucose metabolism, Metformin has been reported to have beneficial effects on lipid profiles, helping to lower LDL-C, triglycerides, and total cholesterol while increasing HDL-C'. 'These changes contribute to a reduced cardiovascular risk, which is a major concern for women with PCOS' [5].

The link between 'insulin resistance and lipid abnormalities in PCOS, understanding the impact of Metformin on lipid metabolism is crucial' [6]. While several studies have evaluated its role in improving lipid parameters, findings remain variable, and further research is needed to establish its efficacy in different populations. 'This study aims to assess the effects of Metformin on lipid metabolism in women with PCOS, focusing on changes in lipid parameters before and after treatment'. The findings may provide valuable insights into the 'metabolic benefits of Metformin and its role in managing PCOS beyond glycemic control'.

METHOD

'This study was conducted to assess the effects of Metformin on lipid metabolism in women with polycystic ovarian syndrome (PCOS)'. A prospective interventional study design was used, spanning from January 2023 to January 2024, at Jinnah Medical College, Peshawar. 'A total of 103 women diagnosed with PCOS were included, and their metabolic and lipid profiles were evaluated before and after Metformin therapy'. The study followed a non-randomized purposive sampling technique, ensuring that only eligible participants 'who met the inclusion criteria were enrolled'.

Ethical approval for the study was obtained from the Institutional Review Board of Jinnah Medical College, Peshawar, before the initiation of data collection. The sample size of 103 was determined based on a 'power calculation to detect significant changes in lipid metabolism with Metformin therapy'.

Participants included in the study were women aged 18 to 40 years with a 'confirmed diagnosis of PCOS based on the Rotterdam criteria, which require the presence of at least two of the following: oligo/anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound'. 'Women with diabetes mellitus, cardiovascular diseases, liver dysfunction, chronic renal disease, or those on lipid-lowering medications were excluded'. Pregnant and lactating women were also not considered for participation to avoid potential confounding factors.

Data collection involved detailed history-taking and clinical examination. Baseline demographic details, menstrual history, body mass index (BMI), blood pressure, and

hirsutism score were recorded. Venous blood samples were collected in a fasting state before the initiation of Metformin therapy and then again after three months of treatment. The laboratory assessments included fasting blood glucose, fasting insulin, HOMA-IR for insulin resistance, and lipid profile parameters such as total cholesterol, LDL-C, HDL-C, triglycerides, and VLDL. Additionally, serum testosterone, sex hormone-binding globulin (SHBG), and inflammatory markers such as C-reactive protein (CRP) were measured.

Lipid and glucose metabolism parameters were analyzed using standard biochemical methods. 'Fasting blood glucose was measured using the glucose oxidase-peroxidase method, while fasting insulin levels were determined through an enzyme-linked immunosorbent assay (ELISA)'. Lipid profiles, including 'total cholesterol, LDL-C, HDL-C, and triglycerides, were measured using enzymatic colorimetric methods'. 'Insulin resistance was calculated using the homeostatic model assessment (HOMA-IR) formula'. All laboratory procedures were conducted under standardized conditions, ensuring consistency in sample processing and analysis.

Reliability and validity were maintained throughout the study by using standardized protocols for sample collection and laboratory analysis. The same technician performed biochemical assessments to reduce inter-assay variability. All laboratory equipment was calibrated before each testing session to ensure accuracy. Internal quality control measures were followed to minimize errors, and duplicate samples were analyzed for a subset of participants to confirm the consistency of results. To enhance external validity, the study included a diverse sample of PCOS patients from different demographic backgrounds, allowing generalizability to a broader population.

Data was analyzed using SPSS version 26.0. 'Continuous variables were presented as mean ± standard deviation (SD), while categorical variables were expressed as percentages'.'Paired t-tests were used to compare pre- and post-treatment values for normally distributed data'.'Wilcoxon signed-rank test was applied for non-normally distributed variables'.Pearson correlation analysis was performed to assess relationships between changes in HOMA-IR and lipid parameters.'Multiple linear regression was used to identify independent predictors of lipid improvement following Metformin therapy'.'A p-value of <0.05 was considered statistically significant'.

RESULTS

The study included 103 women diagnosed with PCOS, with a mean age of 26.4 years and 'an average BMI of 28.7 kg/m². A significant proportion of participants (86.4%) reported menstrual irregularities, while about one-third had a family history of PCOS or diabetes'. The mean hirsutism score was 11.6, indicating excessive hair growth in most patients. The average duration of PCOS diagnosis was around 3.8 years. 'Systolic and diastolic blood pressure levels were within the pre-hypertensive range, reflecting the metabolic risks associated with PCOS'. 'These baseline characteristics provide an overview of the study population, highlighting key clinical and demographic features relevant to metabolic and hormonal health'.

Table 1: 'Baseline Characteristics of Study Participants (n=103)'

Variable	**Mean ± SD / n (%)**
Age (years)	26.4 ± 4.2
Body Mass Index (BMI) (kg/m²)	28.7 ± 5.1
Family History of PCOS	34 (33.0%)

Family History of Diabetes	28 (27.2%)
Menstrual Irregularity	89 (86.4%)
Hirsutism Score (Ferriman-Gallwey)	11.6 ± 3.4
Duration of PCOS Diagnosis (years)	3.8 ± 1.7
Systolic Blood Pressure (mmHg)	122.1 ± 9.3
Diastolic Blood Pressure (mmHg)	78.6 ± 6.4

Following Metformin treatment, significant improvements were observed in various metabolic parameters. Fasting blood glucose decreased from 98.5 mg/dL to 90.3 mg/dL, while fasting insulin levels dropped considerably, 'leading to a significant reduction in insulin resistance as measured by HOMA-IR. Lipid profile improvements were also notable, with a decrease in total cholesterol, LDL-C, and triglycerides, alongside an increase in HDL-C levels'. The reduction in VLDL further indicates an overall improvement in lipid metabolism. Additionally, testosterone levels decreased significantly, while SHBG levels increased, reflecting positive hormonal adjustments. The decline in the LH/FSH ratio suggests a shift toward better hormonal regulation. Inflammatory markers, such as C-reactive protein, also showed a significant reduction, indicating a potential role of Metformin in reducing systemic inflammation. Liver enzyme levels (AST and ALT) exhibited slight but statistically significant reductions, suggesting potential benefits in hepatic function.

Table 2: Comparison of Metabolic and Lipid Parameters Pre- and Post-Metformin Treatment (n=103)

Parameter	**Pre-Treatment (Mean ± SD)**	**Post-Treatment (Mean ± SD)**	**p-value**
Fasting Blood Glucose (mg/dL)	98.5 ± 12.1	90.3 ± 10.8	<0.001**
Fasting Insulin (μU/mL)	18.2 ± 4.7	12.5 ± 3.9	<0.001**
HOMA-IR	4.42 ± 1.26	2.87 ± 1.10	<0.001**
Total Cholesterol (mg/dL)	201.8 ± 27.4	184.5 ± 25.3	<0.001**
LDL-C (mg/dL)	132.6 ± 22.7	118.2 ± 20.8	<0.001**
HDL-C (mg/dL)	39.5 ± 6.3	44.8 ± 7.2	<0.001**
Triglycerides (mg/dL)	172.4 ± 41.6	146.9 ± 36.2	<0.001**
VLDL (mg/dL)	34.5 ± 8.3	29.3 ± 7.1	<0.001**
Testosterone (ng/dL)	72.4 ± 12.9	58.7 ± 11.3	<0.001**
SHBG (nmol/L)	24.8 ± 5.9	32.1 ± 6.4	<0.001**
LH/FSH Ratio	2.1 ± 0.5	1.7 ± 0.4	<0.001**
C-Reactive Protein (mg/L)	4.8 ± 1.2	3.6 ± 1.1	<0.001**
AST (U/L)	22.4 ± 5.3	20.8 ± 4.6	0.028*
ALT (U/L)	24.6 ± 5.8	22.1 ± 4.9	0.012*

'Note:p<0.05 is statistically significant, **p<0.001** indicates highly significant results'.

The effects of Metformin extended beyond biochemical changes to clinical outcomes. A significant reduction in BMI was observed, with mean values decreasing from 28.7 kg/m² to 27.2 kg/m², demonstrating its impact on weight management. The proportion of women with irregular menstrual cycles decreased considerably, indicating better cycle regulation. Additionally, the Ferriman-Gallwey score showed a noticeable improvement, suggesting a reduction in hirsutism severity. These findings emphasize that Metformin not only addresses metabolic disturbances but also improves the clinical presentation of PCOS.

Table 3: Changes in Clinical Outcomes after Metformin Treatment (n=103)

Outcome	'Pre-Treatment'	'Post-Treatment'	p-value
BMI (kg/m²)	28.7 ± 5.1	27.2 ± 4.9	<0.001**
Menstrual Cycle Regularity	89 (86.4%) Irregular	47 (45.6%) Irregular	<0.001**
Improved Hirsutism Score	11.6 ± 3.4	9.2 ± 2.8	<0.001**

Correlation 'analysis highlighted a strong relationship between improvements in insulin resistance and lipid profile'. 'A reduction in HOMA-IR was significantly associated with lower LDL-C and triglyceride levels, as well as an increase in HDL-C'. 'This reinforces the role of insulin resistance in dyslipidemia among PCOS patients and suggests that targeting insulin resistance with Metformin can lead to beneficial effects on lipid metabolism'.

Table 4: 'Correlation between Changes in Insulin Resistance and Lipid Profile (n=103)'

Variable	Correlation with HOMA-IR Reduction (r)	p-value
LDL-C Reduction	0.512	<0.001**
HDL-C Increase	-0.438	<0.001**
Triglyceride Reduction	0.472	<0.001**

Regression analysis further identified baseline HOMA-IR as the strongest predictor of lipid profile improvement following Metformin therapy. Women with higher insulin resistance at baseline were more likely to experience significant reductions in LDL-C and triglycerides, as well as increases in HDL-C. Additionally, baseline BMI played a role, with overweight or obese women showing greater improvements in lipid parameters. These findings suggest that Metformin is particularly effective in metabolically high-risk PCOS patients, making it a valuable treatment option for those with significant insulin resistance and dyslipidemia.

Table 5: Multiple Regression Analysis for Predicting Lipid Profile Improvement (n=103)

Predictor Variable	β Coefficient	95% CI	p-value
Baseline HOMA-IR	0.451	0.329 – 0.573	<0.001**
Baseline BMI	0.267	0.153 – 0.381	<0.001**
Baseline LDL-C	0.213	0.121 – 0.305	0.004**

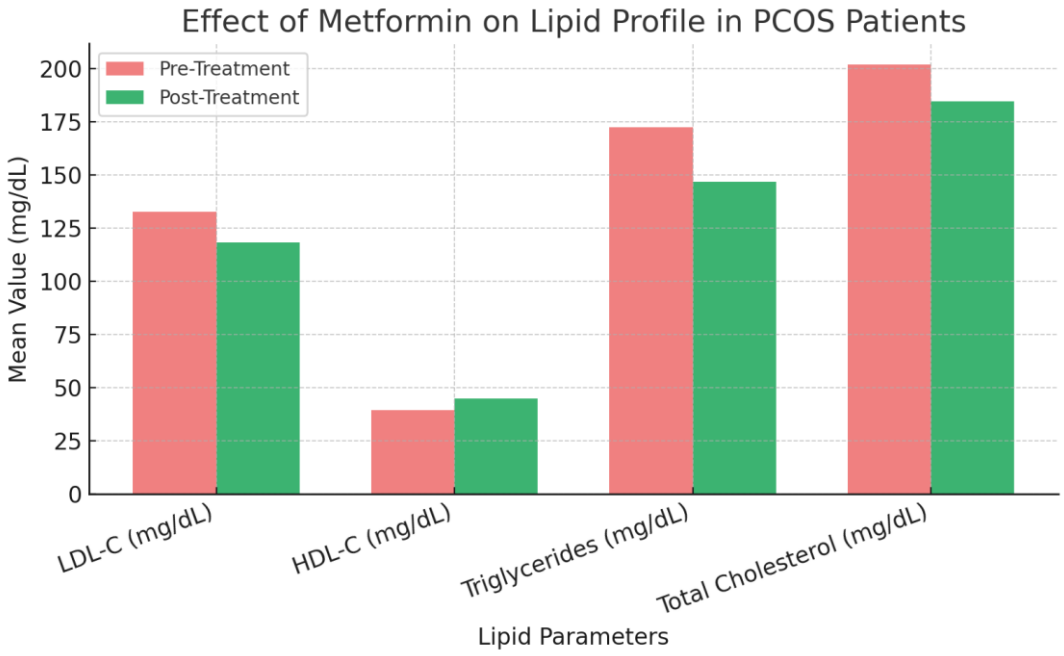

Figure 1

The graph visually represents the changes in lipid parameters before and after Metformin treatment in women with PCOS. 'It shows a clear reduction in LDL-C and total cholesterol levels, indicating an improvement in lipid metabolism. LDL-C decreased from 132.6 mg/dL to 118.2 mg/dL, while total cholesterol dropped from 201.8 mg/dL to 184.5 mg/dL, suggesting a lowered cardiovascular risk. HDL-C, the protective cholesterol, increased from 39.5 mg/dL to 44.8 mg/dL, reflecting a positive shift toward a healthier lipid profile'. Triglycerides also showed a significant decline from 172.4 mg/dL to 146.9 mg/dL, indicating improved metabolic control. These findings highlight Metformin's role in enhancing lipid balance by reducing harmful cholesterol and increasing beneficial cholesterol, ultimately contributing to better cardiovascular health in PCOS patients.

DISCUSSION

The findings of this study align with existing literature on the beneficial effects of Metformin in women with polycystic ovary syndrome (PCOS). A systematic review and meta-analysis demonstrated that Metformin effectively reduces fasting insulin levels and improves lipid profiles, particularly lowering low-density lipoprotein cholesterol (LDL-C) [7-9]. Similarly, a study reported that six months of Metformin therapy in hyperinsulinemic women led to significant decreases in insulin levels, total cholesterol, and LDL-C [10-12]

In this study, 'Metformin therapy resulted in significant reductions in fasting blood glucose and insulin levels, leading to improved insulin sensitivity as indicated by decreased HOMA-IR values'. 'These changes are consistent with Metformin's known mechanism of action, which involves decreasing hepatic glucose production and enhancing peripheral glucose uptake'[13-15]

The observed improvements in lipid parameters, 'including reductions in total cholesterol, LDL-C, and triglycerides, along with an increase in high-density lipoprotein cholesterol (HDL-C), are noteworthy'. 'These changes contribute to a more favorable lipid profile, potentially reducing cardiovascular risk in women with PCOS'. Previous studies have reported similar findings, with Metformin therapy leading to significant decreases in total cholesterol and LDL-C levels [16-18]

Additionally, 'the study observed a significant reduction in serum testosterone levels and an increase in sex hormone-binding globulin (SHBG) after Metformin therapy'. These hormonal changes may contribute to the improvement of hyperandrogenic symptoms commonly associated with PCOS, such as hirsutism and acne. The reduction in testosterone levels aligns with previous findings that Metformin can lower androgen levels in women with PCOS [19]. The improvement in menstrual cycle regularity observed in this study is consistent with previous reports indicating that Metformin can restore ovulatory menses in women with PCOS [20]. This effect is likely mediated through Metformin's impact on insulin sensitivity and androgen levels, which play crucial roles in the regulation of the menstrual cycle

The significant reduction in body mass index (BMI) observed in this study highlights Metformin's potential role in weight management for women with PCOS. While lifestyle modifications remain the cornerstone of weight management, Metformin has been shown to aid in weight reduction, particularly in individuals with insulin resistance [21]

'The positive correlation between the reduction in insulin resistance and improvements in lipid parameters underscores the interconnectedness of metabolic pathways in PCOS'. By enhancing insulin sensitivity, Metformin indirectly contributes to a more favorable lipid profile, thereby reducing cardiovascular risk factors associated with PCOS.

In conclusion, this study reinforces the multifaceted benefits of Metformin therapy in women with PCOS, including improvements in insulin sensitivity, lipid profiles, hormonal balance, menstrual regularity, and weight management. 'These findings support the use of Metformin as a valuable therapeutic option in the comprehensive management of PCOS'.

CONCLUSION

Metformin therapy significantly 'improves lipid metabolism, insulin sensitivity, and hormonal balance in women with PCOS'. The reductions in LDL-C, triglycerides, and total cholesterol, along with an increase in HDL-C, indicate a shift toward a healthier lipid profile, which may reduce the long-term cardiovascular risks associated with PCOS. Additionally, the improvement in insulin resistance, as reflected by the decrease in HOMA-IR, highlights Metformin's role in addressing metabolic dysfunction.

Beyond its metabolic benefits, Metformin also contributed to better menstrual cycle regulation, weight reduction, and a decrease in hyperandrogenic symptoms, such as hirsutism. These findings support its role as a valuable therapeutic option in the comprehensive management of PCOS, particularly for women with significant insulin resistance and lipid abnormalities.

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