

**Research article****Effect of Metformin therapy on lipid profile in obese and non-obese women with polycystic ovarian syndrome (PCOS)****A. Swathi,<sup>1</sup> Vijayalakshmi<sup>2</sup>, I. Yogananda Reddy<sup>3</sup>**<sup>1</sup>Department of Physiology, SVS Medical College, Mahabubnagar, 509001 Telangana, India<sup>2</sup>Department of Physiology, Saveetha Medical College Chennai, 602105, Tamil Nadu, India<sup>3</sup>Department of Physiology, ESIC Medical College, Sanathnagar, Hyderabad, 500028, Telangana, India**(Received: July 2021****Revised: January 2022****Accepted: January 2022)**

Corresponding author: A. Swathi. Email: ASwathiReddy2017@gmail.com

**ABSTRACT**

**Introduction and Aim:** Polycystic ovarian syndrome (PCOS) is the most common endocrine condition affecting the reproductive system in women. It is characterized by obesity, irregular menstruation, anovulation, hirsutism, insulin resistance, and dyslipidemia. Metformin, an oral anti-diabetic drug is known to stabilize metabolic disturbances caused by PCOS. This study aims to determine the effect of metformin therapy on lipid profile in obese and non-obese women with polycystic ovarian syndrome.

**Materials and Methods:** It is a prospective, clinical, interventional study, participated by sixty women aged between 13 to 45 years, suffering with PCOS, who are attending the gynecology outpatient department at SVS medical college and hospital, from a year. The subjects were divided into two groups, Group-1 (Obese women) and Group-2 (non-obese women) and received the anti-diabetic drug, Metformin orally with doses of 500mg/day for a year. Approval of our study was done by Ethical Institutional Board. Demographic parameters age, BMI, and lipid profile including High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), Triglycerides (TAG), & Total Cholesterol (TC) were assessed. SPSS was applied for data analysis and  $p<0.001$  was considered statistically significant.

**Results:** A combined group study of obese and non-obese women subjects showed a BMI decrease in non-obese subjects at 6 months by Metformin therapy. HDL levels increased in non-obese women subjects with a statistical significance. LDL and TAG levels remained unchanged at 6 months by Metformin therapy in both groups. Total cholesterol levels were high in non-obese women and were decreased in the obese women group after Metformin treatment, this metformin therapy could be useful in controlling the metabolic disturbances in non-obese women suffering from PCOS.

**Conclusion:** Metformin has an optimistic physiological effect on the BMI & lipid profile of women suffering from PCOS, hence can help control metabolic disturbances.

**Keywords:** Metformin; polycystic ovarian syndrome; lipid profile; obese and non-obese women.

**INTRODUCTION**

Polycystic ovary syndrome is an endocrine disorder affecting reproductive as well as metabolic features of about 4 to 18% of women in reproducing females (1). Women with PCOS has an atherogenic lipid profile signified by lower HDL (High-Density Lipoprotein) levels and higher TAG (Triglycerides) and LDL (Low-Density Lipoprotein) levels (2). Increased insulin levels because of insulin resistance are noted in PCOS suffering women, which eventually increases androgen levels. Due to the impact of insulin resistance in the PCOS disorder, a common treatment strategy involves insulin sensitizing drugs, like metformin (3).

Metformin, a biguanide is an oral anti-diabetic drug known to improve metabolic abnormalities, in PCOS thereby improving lipid profile, androgen levels, and

menstrual disturbances (4). Earlier medical studies suggested Metformin therapy in the treatment of PCOS, which was found to be effective, as Metformin increases insulin sensitivity and reduces BMI and cholesterol levels (5).

Obesity is the most common observation in PCOS and intensifies many reproductive and metabolic functions. The relationship between obesity and PCOS is complicated (6). Obesity and raised BMI are the clinical features of PCOS and need to be monitored while treating PCOS (7). As the cause of PCOS has not been diagnosed till now, hence its treatment depends on the signs and characteristics of patient (8). The aim of our study is to determine the effect of the metformin therapy on lipid profile in obese and non-obese women with polycystic ovarian syndrome belonging to obese & non-obese category.

## MATERIALS AND METHODS

Our study is a prospective, clinical, interventional study, participated by 60 women with PCOS, attending gynecology outpatient department at SVS medical college and hospital, for one year. They received the anti-diabetic drug, Metformin orally with doses of 500mg/day for a year. The present study was approved by the Institutional Ethical committee/IEC. The study was conducted after obtaining the Informed Consent from the subjects. Demographic parameters age, BMI, and lipid profile were recorded.

### Group allocation

Group 1: Obese women suffering from PCOS.

Group 2: non-obese women suffering from PCOS.

### Inclusion Criteria

1. Age from 13 to 45 yrs.
2. Women diagnosed with PCOS, and selection was based on revised Rotterdam criteria (9).
3. non-diabetic patients

### Exclusion Criteria

1. Pregnant and nursing women.
2. Subjects with renal, liver, thyroid, or gastrointestinal problems.
3. Recent history of major surgeries, trauma.
4. Diabetic patients

### Estimation of metabolic parameters (Lipid profile)

High-density lipoprotein (HDL), ( $\geq 40\text{mg/dL}$ )

Low-density lipoprotein (LDL), ( $<100\text{mg/dL}$ )

Triglycerides (TAG), ( $<150\text{mg/dL}$ )

Total cholesterol (TC), (125 to 200mg/dL), levels were estimated by enzymatic colorimetric methods and calculations (10).

### Statistical analysis

Executed by using the SPSS software and  $p<0.001$  was considered statistically significant. Data analysis was done by statistical tools, a) Descriptive analysis, b) Student's t test, and c) ANOVA.

## RESULTS

Sixty obese and non-obese women participants diagnosed with PCOS were taken. The effect of metformin therapy on the lipid profile of obese and non-obese women with PCOS was studied for 6 months and the following observations were recorded.

In our study, 24-34 years of age group subjects were in majority (46.8%; Fig. 1). BMI calculations of obese and non-obese women suffering from PCOS were done and a combined group study showed a decrease in BMI value of non-obese subjects at 6 months by Metformin therapy was noted. (Fig. 2).

Table1 represents the effect of Metformin on the lipid profile of obese and non-obese women, HDL levels increased in non-obese women ( $3.5\pm 0.2$ ) with a statistical significance ( $p<0.001^*$ ) when compared to obese women ( $2.0\pm 0.2$ ). There was not much difference in the LDL levels of obese ( $2.2\pm 0.3$ ) and non-obese ( $2.1\pm 0.3$ ) women subjects. TAG levels also didn't show a remarkable difference in obese ( $2.5\pm 0.3$ ) and non-obese ( $2.3\pm 0.5$ ) women subjects in the study. Total cholesterol levels were raised in the non-obese women ( $6.5\pm 0.1$ ) when compared to the obese women ( $5.0\pm 0.4$ ) but was not statistically significant.

**Table 1:** Effect of Metformin on the lipid profile of obese and non-obese women

Lipid profile	Obese women (n=30)	Non- obese women (n=30)	p value
HDL levels	$2.0\pm 0.2$	$3.5\pm 0.2$	0.001*
LDL levels	$2.2\pm 0.3$	$2.1\pm 0.3$	0.115
TAG levels	$2.5\pm 0.3$	$2.3\pm 0.5$	0.176
TC levels	$5.0\pm 0.4$	$6.5\pm 0.1$	0.127

Data represented as Mean $\pm$  SD, SD- standard deviation,

\*statistical significant (p value <0.001). High-density

lipoprotein (HDL), Low-density lipoprotein (LDL),

Triglycerides (TAG), Total cholesterol (TC)

Table 2 represents combined group study of subjects, Metformin therapy on obese women showed HDL baseline value  $1.5\pm 0.2$  and at 6<sup>th</sup> month  $2.1\pm 0.2$  and on non-obese women, HDL baseline value was  $2.2\pm 0.2$  and at 6<sup>th</sup> month  $2.6\pm 0.2$ , there was an increase, with a statistical significance ( $p<0.001^*$ ) in this group as well. LDL values were unchanged in both the study groups. In the obese group baseline value was  $3.0\pm 0.2$  and at 6<sup>th</sup> month was  $3.1\pm 0.2$ . In the non-obese group baseline value was  $2.5\pm 0.2$  and at 6<sup>th</sup> month was  $2.7\pm 0.2$  and no statistical significance was found. TAG levels also didn't represent any major change, in the obese group baseline value was  $1.7\pm 0.1$  and at 6<sup>th</sup> month was  $1.8\pm 0.2$ . In the non-obese group baseline value was  $2.6\pm 0.2$  and at 6<sup>th</sup> month was  $2.8\pm 0.2$  with no statistical significance. Total cholesterol remained unchanged in the obese women group, baseline value was  $5.4\pm 0.3$  and at 6<sup>th</sup> month was  $5.5\pm 0.2$ . Total cholesterol levels were high in non-obese women,

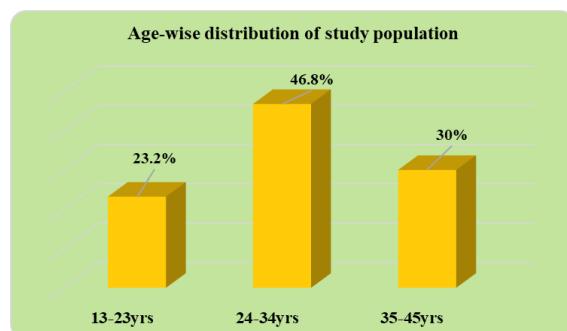
baseline value was  $4.6 \pm 0.2$  and at 6<sup>th</sup> month ( $5.0 \pm 0.2$ ) after Metformin treatment.

**Table 2:** Effect of Metformin on the lipid profile of obese and non-obese women before and after treatment

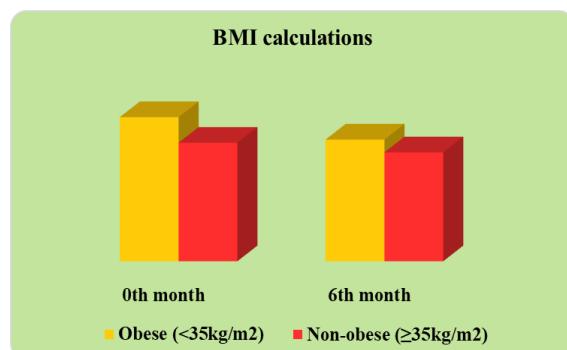
Lipid profile	Metformin therapy on obese women		Metformin therapy on non- obese women	
	0 <sup>th</sup> month	6 <sup>th</sup> month	0 <sup>th</sup> month	6 <sup>th</sup> month
HDL levels	$1.5 \pm 0.2$	$2.1 \pm 0.2^*$	$2.2 \pm 0.2$	$2.6 \pm 0.2^*$
LDL levels	$3.0 \pm 0.2$	$3.1 \pm 0.2$	$2.5 \pm 0.2$	$2.7 \pm 0.2$
TAG levels	$1.7 \pm 0.1$	$1.8 \pm 0.2$	$2.6 \pm 0.2$	$2.8 \pm 0.2$
TC levels	$5.4 \pm 0.3$	$5.5 \pm 0.2$	$4.6 \pm 0.2$	$5.0 \pm 0.2$

Data represented as Mean $\pm$ SD, SD- standard deviation,  
\*statistical significance (p value  $<0.001$ ).

High-density lipoprotein (HDL), Low-density lipoprotein (LDL), Triglycerides (TAG), Total cholesterol (TC)



**Fig. 1:** Age-wise distribution of obese and non-obese women suffering from PCOS



**Fig. 2:** BMI calculations of obese and non-obese women suffering from PCOS

## DISCUSSION

Most of the women subjects with PCOS were from the age group 24-34 years (46.8%), which is as per the other studies too (11,12), where women displayed PCOS between age group 16- 38 years and with advancing age. The BMI calculations showed a decrease in non-obese women subjects at 6 months by metformin therapy. A similar study by Guan *et al.*, (13), revealed Metformin to be an efficient drug for women with PCOS.

With metformin therapy, HDL levels were increased significantly at the end of 6 months study suggesting metformin therapy to be a good line of treatment in obese and non-obese women with PCOS. Cheang *et al.*, (14), showed metformin improved the metabolic disturbances of women with PCOS, particularly in HDL cholesterol.

The LDL and TAG level remained unchanged at 6 months by Metformin therapy in both obese and non-obese PCOS study groups, and was comparable to the study done by Karimzadeh *et al.*, (15).

The total cholesterol levels were high in non-obese women with PCOS and remained unchanged in the obese women with PCOS, after the treatment with metformin. Rautio *et al.*, (16) study is also in favor of Metformin therapy in not changing total cholesterol levels in women with PCOS.

## CONCLUSION

Metformin has an optimistic and beneficial effect on the lipid profile and BMI of women suffering from PCOS hence can help control metabolic disturbances.

## ACKNOWLEDGEMENT

Deepest gratitude to Dr. Naima Fatima, Professor & Head, Department of Gynecology, SVS Medical College and Hospital for being abundantly helpful and supportive.

## CONFLICT OF INTEREST

Authors declare no conflict of interest.

## REFERENCES

1. Sirmans, S.M., Pate, K.A. Epidemiology, diagnosis, and management of polycystic ovary syndrome. *Clinical Epidemiology*. 2013;6(1):1-13.
2. Talbott, E., Clerici, A., Berga, S.L., Kuller, L., Guzick, D., Detre, K., *et al.*, Adverse lipid and coronary heart disease risk profiles in young women with polycystic ovary syndrome: Results of a case-control study. *Journal of Clinical Epidemiology*. 1998;51(5):415-422.
3. Önalan, G., Pabuçcu, R., Goktolga, U., Ceyhan, T., Bagis, T., Cincik, M., *et al.*, Metformin treatment in patients with polycystic ovary syndrome undergoing in vitro fertilization: A prospective randomized trial. *Fertility and Sterility*. 2005;84(3):204-211.

4. Macut, D., Bjekić-Macut, J., Rahelić, D., Doknić, M. Insulin and the polycystic ovary syndrome: Diabetes Research and Clinical Practice. 2017;130: 163-170.
5. Knochenhauer, E.S., Key, T.J., Kahsar-Miller, M., Waggoner, W., Boots, L.R., Azziz, R., *et al.*, Prevalence of the polycystic ovary syndrome in unselected black and white women of the Southeastern United States: A prospective study: Journal of Clinical Endocrinology and Metabolism. 1998;83(9):3078-3082.
6. Sam, S. Obesity, and polycystic ovary syndrome: Obesity Management. 2007;3(2):69-73.
7. Beydoun, H.A., Stadtmauer, L., Beydoun, M.A., Russell, H., Zhao, Y., Oehninger, S., *et al.*, Polycystic ovary syndrome, body mass index and outcomes of assisted reproductive technologies: Reproductive BioMedicine Online. 2009;18(6):856-863.
8. Ajossa, S., Guerriero, S., Paoletti, A.M., Orrù, M., Melis, G.B. The treatment of polycystic ovary syndrome: Minerva Ginecologica. 2004;56(1):15-26.
9. Azziz, R. Diagnosis of polycystic ovarian syndrome: The Rotterdam criteria are premature: Journal of Clinical Endocrinology and Metabolism. 2006;91(3):781-785.
10. Mizoguchi, T., Edano, T., Koshi, T. A method of direct measurement for the enzymatic determination of cholestryly esters: Journal of Lipid Research. 2004;45(2):396-401.
11. Mehandiratta, R., Jindal, P., Takkar, V., Kapila, P.T., Kapila, R. Effect of Administration of Metformin on Lipid Profile in Patients with Polycystic Ovary Syndrome after Six Months of Treatment: International Journal of Medical Research Professionals. 2016;2(5):66-69.
12. Mellembekken, J.R., Berga, S.L., Kilen, M., Tanbo, T.G., Byholm, T., Fedorcsák, P., *et al.*, Sustained fertility from 22 to 41 years of age in women with polycystic ovarian syndrome: Human Reproduction. 2011;26(9):2499-2504.
13. Guan, Y., Wang, D., Bu, H., Zhao, T., Wang, H. The Effect of Metformin on Polycystic Ovary Syndrome in Overweight Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. International Journal of Endocrinology. 2020;1-12.
14. Cheang, K.I., Huszar, J.M., Best, A.M., Sharma, S., Essah, P.A., Nestler, J.E., *et al.*, Long-term effect of metformin on metabolic parameters in the polycystic ovary syndrome: Diabetes and Vascular Disease Research. 2009;6(2):110-119.
15. Karimzadeh, M.A., Eftekhar, M., Taheripanah, R., Tayebi, N., Sakhavat, L., Zare, F., *et al.*, The effect of administration of metformin on lipid profile changes and insulin resistance in patients with polycystic ovary syndrome: Middle East Fertility Society Journal. 2007;12(3):174-178.
16. Rautio, K., Tapanainen, J.S., Ruokonen, A., Morin-Papunen, L.C. Effects of Metformin and ethinyl estradiol-cyproterone acetate on lipid levels in obese and non-obese women with polycystic ovary syndrome: European Journal of Endocrinology. 2005;152(2):269-275.