

**Research Article**

**Efficacy of Metformin in Women with PCOS and to Compare  
in Non-Obese and Obese Women**

**<sup>1</sup>Sadaf Ali Raja, <sup>2</sup>Sarwat Ali Raja  
and <sup>3</sup>Naeem Mubarak**

<sup>1</sup>Lahore General Hospital, Lahore

<sup>2</sup>Associate Professor, Ph. D, Pharmacology & Toxicology, Lahore Pharmacy College, Lahore

<sup>3</sup>Associate Professor, Phd, Pharmacology Practice, Lahore Pharmacy College, Lahore

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**ABSTRACT**

**OBJECTIVES:** The objective of the study was:

- To determine the efficacy of metformin in women with PCOS and to compare the efficacy of metformin in non-obese and obese women with polycystic ovarian syndrome

**SETTINGS:** Lahore General Hospital, Lahore

**DURATION OF STUDY:** April 2017 to April 2018

**RESULTS :** Comparison of ovulation reveals significant difference between obese and non-obese groups, 83.14%(n=281) in non-obese group and 32.25%(n=109) were ovulated while menstrual was achieved in 62.43%(n=211) in Group-A and 53.55%(n=181) in Group-B, the final outcome efficacy in both groups was recorded, where efficacy in Group-A was recorded in 83.14%(n=281) and 53.55%(n=181) was in Group-B, p value was calculated as 0.000 which shows a significant difference in both groups.

**CONCLUSION:** The results of the study conclude that comparison between the groups was found to be statistically significant with regards to ovulation and menstrual regularity in both groups. Metformin monotherapy is very effective in improving ovulation and pregnancy rates in lean women with PCOS as compared with obese women.

**KEY WORDS:** Polycystic Ovarian Syndrome, Obese, non-obese, Metformin, efficacy

**INTRODUCTION**

The polycystic ovary syndrome (PCOS) is a commonly experienced endocrine problem in women of reproductive age accounting 5–10 %.<sup>1</sup> It is a combination of complex disorders with multiple components, including reproductive, metabolic, and cardiovascular manifestations leading to long-term health concerns that cross the life span<sup>2</sup>. The diagnostic criteria for PCOS are

insulin resistance, ovarian dysfunction evidenced by an-ovulation, oligomenorrhea or amenorrhea and clinical evidence of androgen excess (e.g., hirsutism and acne) in the absence of other conditions that can cause these same symptoms.<sup>3</sup> Menstrual irregularities, an-ovulation and infertility are common and distressing sequel of PCOS.

The use of insulin sensitizers like metformin, for the improvement of insulin resistance is considered to be of therapeutic value directly or indirectly in the management of PCOS.<sup>4,5</sup>

Since not all PCOS patients are obese or insulin resistant, it is not clear whether PCOS patients without insulin resistance also benefit from insulin sensitizers. Several studies have suggested a positive effect of metformin and short term trials on the effects of insulin sensitizing drugs have shown promising role in the improvement of insulin sensitivity, reduction of insulin secretion and regularization of menstrual cycles resulting in increased ovulation and fertility rates.<sup>2</sup> Regarding ovulation Kumari AS and co-workers showed that in non-obese and obese groups 15/17 women (88%) and 5/17 women (29%) ovulated resultantly comparison between the groups was found statistically significant.<sup>6</sup> Another study by Tan S and co-workers showed that menstrual regularity was achieved in 59% of non-obese PCOS women as compared to 50% of obese women with PCOS.<sup>7</sup> The results of this study will help to clarify the comparative efficacy of metformin in correcting menstrual irregularity and ovulation in non-obese versus obese women with polycystic ovary syndrome. It will therefore help in better management of women with polycystic ovary syndrome having different body mass indices.

## METHODOLOGY

In this study a total of Six hundred and seventy six (676) patients admitted through gynecology outpatient department were recruited. We enrolled all the obese and non- obese women with PCOS coming to the gynecology OPD of our department, having no other known systemic disease whereas all females with peri-climacteric gonadotrophin values, hyperprolactinaemia, hormonal treatment, pregnancy or lactation were excluded. Two groups were formed, Group-A was allotted to the non-obese, and Group-B was to the obese PCOS patients. Hormonal profile including day 2 serum FSH, LH, Prolactin, testosterone and mid-luteal phase progesterone was carried out. Ultrasound

examination of pelvis was carried out in all patients. Metformin therapy was started at an oral dose of 500mg/ day for one week, then twice a day for another week and then was maintained at 1500 mg/ day for 6 months in non- obese women. The dose was increased to 1000mg twice a day in obese women. Follow up was ensured by taking contacts of patients, trainee researcher ensured this. All women were reviewed every two months to look for compliance and any other concerns. Detailed clinical, biochemical and ultrasound examination were repeated after 6 months. Ovulation and menstrual regularity was documented after six months of administration of metformin and all findings were noted on the Performa. The data analysis was done on SPSS where mean and standard deviation was calculated for quantitative variables like age and BMI. Frequencies and percentages were calculated for qualitative variables like menstrual regularity and ovulation. Chi square test was used to compare the efficacy of metformin in both groups. P- value of < 0.05 was considered statistically significant.

## RESULTS

Age distribution of the patients reveals that the age range was 20-40 years, common age was calculated in Group-A as  $28.23 \pm 3.41$  and  $27.45 \pm 4.58$  in Group-B, majority of the patients in both groups were between 26-30 years, 40.53% (n=137) in Group-A and 42.90% (n=145) in Group-B, 28.11% (n=95) between 31-35 years in Group-A and 25.74% (n=87) in Group-B, 18.64% (n=63) in Group-A and 16.86% (n=57) in Group-B between 35-40 years of age while 12.72% (n=43) in Group-A and 14.50% (n=49) in Group-B were between 20-25 years of age. (Table No. 1)

Comparison of ovulation was done to know the significance between obese and non-obese groups, 83.14% (n=281) in non-obese group and 32.25% (n=109) were ovulated while 16.86% (n=57) in non-obese and 67.75% (n=229) were not ovulated. P value was calculated as 0.00. (Table No.2)

Comparison of menstrual regularity in both groups was also done where 62.43%(n=211) in Group-A and 53.55%(n=181) in Group-B subjects achieved menstrual regularity while 37.575%(n=127) in Group-A and 46.45%(n=157) were not recorded with menstrual regularity. P value was calculated as 0.019.(Table No.3)

The final outcome efficacy in both groups was recorded and presented in Table No. 4, where efficacy in Group-A was recorded in 83.14%(n=281) and 53.55%(n=181) was in Group-B, p value was calculated as 0.000 which shows a significant difference in both groups. (Table No. 4)

**TABLE No. 1:** Age Distribution Of The Patients (n=676)

Age (in years)	Group-A (n=338)		Group-B (n=338)	
	No. of patients	%	No. of patients	%
20-25	43	12.72	49	14.50
26-30	137	40.53	145	42.90
31-35	95	28.11	87	25.74
35-40	63	18.64	57	16.86
<b>Total</b>	<b>338</b>	<b>100</b>	<b>338</b>	<b>100</b>
<b>Mean and sd</b>	<b>28.23± 3.41</b>		<b>27.45± 4.58</b>	

**TABLE No. 2:** comparison of ovulation in both groups (n=676)

OVULATION	Group-A (n=338)		Group-B (n=338)	
	No. of patients	%	No. of patients	%
Yes	281	83.14	109	32.25
No	57	16.86	229	67.75
<b>Total</b>	<b>338</b>	<b>100</b>	<b>338</b>	<b>100</b>

P value= 0.00

**TABLE No. 3:** comparison of menstrual regularity in both groups (n=676)

Menstrual regularity	Group-A (n=338)		Group-B (n=338)	
	No. of patients	%	No. of patients	%
Yes	211	62.43	181	53.55
No	127	37.57	157	46.45
<b>Total</b>	<b>338</b>	<b>100</b>	<b>338</b>	<b>100</b>

P value= 0.019

**TABLE No. 4:** comparison of efficacy in both groups (n=676)

Efficacy	Group-A (n=338)		Group-B (n=338)	
	No. of patients	%	No. of patients	%
Yes	281	83.14	181	53.55
No	57	16.86	157	46.45
<b>Total</b>	<b>338</b>	<b>100</b>	<b>338</b>	<b>100</b>

P value= 0.000

**DISCUSSION**

The current study was planned to clarify the comparative efficacy of metformin in correcting menstrual irregularity and ovulation in non-obese versus obese women with polycystic ovary syndrome so that the results may help in better

management of women with polycystic ovary syndrome having different body mass indices. In our study, common age was calculated as 28.23±3.41 and 27.45±4.58 in Group-A & B respectively, majority of the patients in both groups were between 26-30 years of age,

comparison of ovulation reveals significant difference between obese and non-obese groups, 83.14%(n=281) in non-obese group and 32.25%(n=109) were ovulated while menstrual was achieved in 62.43%(n=211) in Group-A and 53.55%(n=181) in Group-B.

This finding is in agreement with a study conducted by Stefano Palomba in 2006,<sup>8</sup> where the age was  $26.0 \pm 2.7$ .

The improvement of gonadotrophins level is seen in the study conducted by Stefano Palomba in 2006,<sup>9</sup> where LH/FSH have been reduced; and patients started ovulation, this agreement with the findings of our study improves the credibility of the current trial.

Our results are in agreement with the study conducted by Kumari AS and co-workers who recorded that in non-obese and obese groups 15/17 women (88%) and 5/17 women (29%) ovulated resultantly comparison between the groups was found statistically significant.<sup>6</sup> Another study by Tan S and co-workers showed that menstrual regularity was achieved in 59% of non-obese PCOS women as compared to 50% of obese women with PCOS.<sup>7</sup> While there is no difference between non-obese and obese patients in some studies,<sup>10</sup> others have not been able to demonstrate insulin resistance in lean PCOS women.<sup>11-13</sup> Obesity clearly aggravates the symptoms of PCOS,<sup>10,14</sup> and weight loss is central in the treatment. Weight loss has been shown to enhance ovulation frequency and improve menstrual cyclicality and endocrine profile.<sup>15</sup> It is also considered of fundamental importance in reducing the cardiovascular risk factors included in the metabolic syndrome. Metformin decreases feeling of hunger during hypoglycaemia,<sup>16</sup> and moderate weight loss is common during metformin treatment, but the conclusions of randomized studies differ with regard to the effect of metformin on weight in PCOS.

The results of the study clarifies the comparative efficacy of metformin in correcting menstrual irregularity and ovulation in non-obese and obese women with polycystic ovary syndrome, though

ovulation was significantly higher in non-obese women while the menstrual irregularity was equally rectified in both groups. So, the metformin may be used in both obese and non-obese women as first line therapy for PCO.

## CONCLUSIONS

The results of the study conclude that comparison between the groups was found to be statistically significant with regards to ovulation and menstrual regularity in both groups. Metformin monotherapy is very effective in improving ovulation and pregnancy rates in lean women with PCOS as compared with obese women.

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**COMPARISON OF EFFICACY OF METFORMIN IN OBESE AND NON-OBESE WOMEN  
WITH POLYCYSTIC OVARY SYNDROME (PCOS)  
PERFORMA**

**Group A: Non-Obese**  
**Group B: Obese**

Serial No: \_\_\_\_\_ Date: \_\_\_\_\_

Hospital Reg. No: \_\_\_\_\_

Name: \_\_\_\_\_ D/O;W/O: \_\_\_\_\_

Age(Years): \_\_\_\_\_ Address: \_\_\_\_\_

Telephone No: \_\_\_\_\_

Group: \_\_\_\_\_ Case No.: \_\_\_\_\_

	PRE-TREATMENT	POST- TREATMENT
Menstrual cycles	_____	_____
<b>INVESTIGATIONS</b>	<b>RESULTS</b>	
	PRE-TREATMENT	POST- TREATMENT
BMI	_____	_____
Day 2 Serum FSH	_____	_____
Day 2 Serum LH	_____	_____
Mid-luteal phase progesterone	_____	_____
Ultrasound Pelvis	_____	_____