

The Effect of Metformin on Serum Lipids in Overweight and Obese Patients with Polycystic Ovary Syndrome

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ABSTRACT:

BACKGROUND:

Polycystic ovary syndrome is a very common condition affecting 4% to 18% of women. Polycystic ovary syndrome is associated with metabolic features and diabetes and cardiovascular disease.

OBJECTIVE:

To evaluate the effect of metformin on serum lipids in overweight and obese women with polycystic ovary syndrome.

METHODS:

An observational prospective study conducted at AL- Diwanyia Maternity and child Hospital from May 2011 to March 2013. All women in this study have BMI >27 (range) so, they are all overweight and obese .The women randomized into two group; one group were received metformin therapy for 4 months duration and the other group were kept on no therapy and followed for the same period. All studied women were subjected to measurement of fasting Blood sugar, and measurement of overnight fasting lipid profile which include total cholesterol, triglycerides, high density lipoprotein cholesterol and low density lipoprotein cholesterol.

RESULTS:

For women who received metformin, there was significant increase in the level of high density lipoprotein P = 0.04. The value of triglyceride although decreased after metformin treatment, the difference was not significant P > 0.05.

Other parameters (cholesterol, low density lipoprotein cholesterol) showed no difference. Fasting blood sugar was not changed during the study.

CONCLUSION:

Metformin have been shown to improve the lipid profiles leading to increase the high density lipoprotein cholesterol, the main predictive of cardiovascular disease in the women with polycystic ovary syndrome.

KEYWORDS: polycystic ovary syndrome, metformin, serum lipids.

INTRODUCTION:

Polycystic ovary syndrome (PCOS) is the most common metabolism and endocrine disorders affecting 5-10% of women in their reproductive age. It occurs amongst all races and nationalities, and is a leading cause of infertility. It's main feature are lack of regular ovulation and excessive amount or effect of androgenic hormones^(1, 2, 3). While the causes of PCOS are still unknown, insulin resistance secondary to obesity is strongly correlated to this syndrome^(3, 4).

In 2003 a consensus workshop sponsored by ESHRE / ASRM in Rotterdam indicated PCOS to be present if 2 out of 3 criteria are met:

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1-Oligovulation and / or anovulation.

2-Excess androgen activity.

Polycystic ovaries (by gynaecologic ultrasonography, >12 follicles 2-9mm. at periphery of the ovary and / or increased ovarian volume > 10 ml). This definition, however not to be applied to women on the oral contraceptive pills as it changes the ovarian morphology, it was also suggested that in the presence of dominant follicles (>10mm) or a corpus luteum, the scan was to be repeated in the next cycle.^(4, 5, 6).

Obesity increases hyperandrogenism, hirsutism, and infertility and pregnancy complications both independently and by exacerbating PCOS. In general populations, obesity and insulin resistance further increase type 2 diabetes (DM2) and cardiovascular disease (CVD). Likewise, in

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PCOS obesity worsens insulin resistance and exacerbates reproductive and metabolic features⁽⁷⁾. Furthermore, women with PCOS have increased risk factors for DM2 and CVD, increased impaired glucose tolerance (IGT), DM2 and potentially increased CVD⁽⁸⁾

Metformin, a biguanide antihyperglycemic drug has been used in treatment of type 2 diabetes mellitus, and in diabetic patients, metformin treatment has been shown to have a beneficial effect on circulating lipid level by decreasing the plasma level of triglycerides and total and LDL cholesterol and increasing the level of HDL cholesterol independently of the improvement of glycemic control⁽⁹⁾. However there are only a few studies specifically concerning the effect of metformin therapy on lipid profile in women with PCOS^(10, 11). Metformin is offered as first line treatment to clomiphene resistant women with PCOS.^(11, 12)

PATIENTS AND METHODS:

This is an observational prospective study was conducted at AL- Diwanya Maternity and child Hospital from May 2011 to March 2013. A total of 96 women of age range 18-42 years were included in the study. Detailed history was taken from every participating patient including menstrual history, history of infertility and obstetric history, in addition thorough physical examination beside measuring blood pressure and body mass index (BMI: weight in kilogram / height (meters²){overweight 25 – 29, obese > 30 }) All the women were euthyroid clinically and none had taken medication to affect plasma level of lipids for at least 3 months before the start of the study . Pregnancy or possibility of pregnancy and nursery (lactating), significant liver impairment or renal impairment, neoplasm and cardio vascular disease were considered as exclusion criteria. All studied women were subjected to measurement of fasting Blood sugar,

and measurement of overnight fasting lipid profile which include total cholesterol (TC), triglycerides (TG), HDL cholesterol and LDL-cholesterol and the readings considered as a base line measurements. The women were randomized after above assessment into 2 groups:

Group one: Consist of 40 patients who were put on metformin therapy for 4 months duration.

The metformin dose was 500 mg twice daily for one week and increased to 850 mg twice daily for the rest of 4months follow up in order to improve compliance and tolerance.

Group 2: Consist of 56 women were kept on no therapy and followed up for a period of 4 months (informing patients not take any drug until four months to repeat investigations).

At the end of follow up period over night fasting total serum cholesterol, triglycerides, HDL cholesterol and LDL cholesterol assay were determined. Fasting blood sugar also checked. In the first group 10 of 40 patient were excluded from the study because of gastro intestinal side effects and one patient who received metformin conceived and withdraw from the study. In the second group (control) 16 of 56 patient excluded because of their own desire and were abandoned from the study.

SPSS version 13 was used to do the appropriate statistical tests. The results are expressed as means and standard deviation. Differences were considered to be statistically significant if p-value was <0.05.

RESULTS:

There were no statistically significant difference noted between the two groups of women regarding the age and BMI. i.e. both groups were identical the mean age was (30.5 ± 45) .

All women in this study have BMI >27 so, they are all overweight and obese with PCOS. Table 1.

Table 1: The demographic character of women included in this study.

Characters of the women	Group 1 No. =30	Group 2 No. = 40	Total No. =70	P value
Age (mean range ± SD)	30.4 ± 3	30.6 ± 7	30.5 ± 45	0.45
BMI (kg/m2) (mean range ± SD)	28.1 ± 62	29.2 ± 3	28.65 ± 41	0.42

Table 2 shows an increase in the percentage of

infertility, hirsutisim and acne in both groups as it is expected in patients with PCOS.

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Table 2: The clinical presentations of women in both groups.

Presentation of the PCOS women	Group 1 No. =30	Group 2 No. = 40	Total No. =70
Infertility	27 (90%)	40 (100%)	67 (957%)
Hirsutisim	23 (76.7%)	34 (85%)	57 (81.4%)
Acne	24 (80%)	33 (82.5%)	57 (81.4%)

Serum level of total cholesterol, triglyceride, LDL cholesterol, HDL cholesterol and fasting blood sugar were comparable in both groups of the patients at the base line readings, and there

was no significant difference between both groups $P > 0.05$.

Table 3 shows the values of serum lipids in both groups were generally increased or at upper normal limits with HDL level below normal.

Table 3: Lipid profiles of women in both groups at baseline.

Parameter mg/dl	Group 1 No. =30	Group 2 No. =40	P – value
Cholesterol	208.31 ± (24.7)	212.5 ± (30.1)	P = 0.2
HDL - Cholesterol	54.9 ± (11.8)	52.7 ± (88)	P = 0.12
LDL – Cholesterol	108.7 ± (27.5)	123.19 ± (33.5)	P = 0.14
Triglyceride	167.2 ± (40.5)	172.3 ± (38)	P = 0.1
F.B.S.	111.3 ± (18.4)	107.6 ± (20.9)	P = 0.15

Table 4 shows the serum levels of lipid in the two study groups HDL cholesterol increase in women received metformin. There was

significant difference in HDL Cholesterol level between the two groups. Other parameter show no significant differences.

Table 4: Lipid profiles comparison between the study groups at 4 months follow up.

Parameter mg/dl	Group 1 (No. =30)	Group 2 (No. =40)	P. values
Cholesterol	210.43 ± 31.2	212.11 ± 26.3	P = 0.2
HDL - Cholesterol	59.82 ± 19.5	50.34 ± 9.4	P =0.04
LDL- Cholesterol	118.2 ± 31.3	120.92 ± 13.5	P = 0.2
Triglyceride	155.61 ± 22.7	170.29 ± 47.5	P = 0.06
Fasting BG.	103.9 ± 12.2	111.2 ± 9.5	P = 0.5

Table 5 shows the difference in serum lipid in the study group 1 before and after metformin treatment. There was a significant difference in HDL cholesterol. The values of Triglyceride although decreased after metformin treatment,

the difference was not significant. Other parameters (cholesterol, LDL) show no difference. Fasting blood sugar not changed during the study.

Table 5: Lipid profile comparison in the study group 1.

Parameter mg/dl	Metformin		P. values
	0 month	4 month	
Cholesterol	208.31 ± 24.7	210.43 ± 31.2	P = 0.2
HDL - Cholesterol	54.9 ± 11.8	59.82 ± 19.5	P = 0.04
LDL- Cholesterol	108.7 ± 77.5	118.2 ± 31.3	P = 0.1
Triglyceride	167.2 ± 40.5	155.61 ± 22.7	P = 0.1
Fasting Blood glucose	111.3 ± 18.4	103.9 ± 12.2	P = 0.2

DISCUSSION:

Poly cystic ovary syndrome (PCOS) is a common disorder, with estimates of the prevalence lying between 5-10% of women^(3, 13). In women, cardio vascular disease is the most common cause of death, and these with polycystic have 7.4 fold relative risk for myocardial infarction calculated by risk factor analysis due to the prevalence of the glucose intolerance, hypertension, insulin resistance, central obesity and dyslipidemia^(14, 15). The latter is characterized by low HDL cholesterol and raised triglycerides and may explain their cardio vascular risk particularly as low high density lipoprotein (HDL) cholesterol appears to be the most important lipoprotein predictor of CVD in women^(16,17).

Approximately 70-80% of PCOS patients are obese. In this study, the whole women were overweight and obese with BMI > 28. It is well known from previous studies that obesity is associated with insulin resistance, however, PCOS patients have evidence of insulin resistance beyond that of obese women in the general population^(6, 11, 18).

The base line observations within study regarding the serum lipids level and fasting blood glucose correspond with previous study which shown that obese patient with PCOS have serum level of HDL, LDL triglyceride and total cholesterol correlated significantly with insulin resistance. These results strengthen the concept that obesity and insulin resistance are main contributors to the development of lipid metabolic disturbance^(19, 20, 21).

The current study shows that metformin treatment significantly increased serum HDL cholesterol in study group 1, Triglyceride is

decreased in the treatment group but the difference was not significant between the two groups. In addition metformin treatment show no difference in other parameters of lipid profile (LDL, and total cholesterol) and fasting blood glucose. These results corresponds with result obtained by Krautio et. al. Other studies done by, Ehermann et al and velazquez et al shown only a negligible or no effect on serum lipids in women with PCOS. These discrepancies in the result among researches could be explained by difference in the studied population or by shorter duration of treatment.^(19, 20, 21) It has been found by some studies done by Morin- papunen et al and Glueck et al that the beneficial effect of metformin on serum lipids is related to the duration and the dosage of the treatment. This beneficial effect was observed after 3months of treatment and at a dosage of 1g/day.^(22, 23, 24)

The current study results of positive effect of metformin treatment on lipid profiles in PCOS patients was also corresponding with the results obtained by Wild et al, Gordon et al and Mohamed et al whose researches were mainly to study the relationships of BMI and serum lipids profiles in PCOS patients.^(22, 23, 24, 25)

CONCLUSION:

Metformin – insulin sensitizers have been shown to improve the lipid profiles leading to increase the HDL cholesterol, the main predictive of cardio vascular disease in the women with PCOS.

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