

ORIGINAL ARTICLE

# The Effect of Bariatric Surgery on Polycystic Ovary Syndrome (PCOS) Symptoms and Related Hormones Improvement in Women with Morbid Obesity

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## ABSTRACT

**Background:** Obesity is associated with developing polycystic ovary syndrome (PCOS). The present study investigated whether weight loss after bariatric surgery could improve symptoms and related hormones in women with morbid obesity.

**Methods:** In a prospective observational study, 50 women aged 18-40 years with body mass index (BMI)=42.3 kg/m<sup>2</sup> who underwent laparoscopic Roux-en-Y gastric bypass (RYGB) were enrolled. Evaluation of anthropometric data, serum testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), fasting plasma glucose (FPG), and lipid profile were measured preoperatively and at 1-year follow-up

**Results:** Of 50 women, 32 (64%) women were diagnosed to have PCOS. The mean BMI at 1-year follow-up was 27.05 kg/m<sup>2</sup>. Hirsutism and irregular menstruation resolved entirely among 68.8% (11/16) and 100% (18/18) at 1-year follow-up. There was a significant decrease in total serum testosterone (2.1±0.2 to 0.9±0.1 ng/mL) and LH (8.5±3.36 to 5.02±2.4 mIU/mL) at 1-year follow-up, whether changes in levels of serum FSH, PRL were not significant.

**Conclusion:** Bariatric surgery was effective in weight loss and improvement of PCOS symptoms and related hormones in women with morbid obesity. Thus, women with PCOS and morbid obesity should be eligible for bariatric surgery.

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## Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy affecting women of reproductive age and is characterized by ovulation dysfunction, hyperandrogenism, and polycystic

ovarian morphology (PCOM). The prevalence of PCOS ranges from 8% to 13% depending on the diagnostic criteria and study population (1, 2). Women with PCOS exhibit menstrual irregularities, hirsutism, and infertility. In addition, this syndrome

can lead to long-term comorbidities, including obesity, type 2 diabetes mellitus (DM), cardio metabolic diseases, endometrial carcinoma, and psychological disorders (3-5). Obesity is also associated with the development and progression of polycystic ovary syndrome (PCOS) and the prevalence of obesity in patients with PCOS is about 50% (6). Bariatric surgery is a highly effective treatment option for obese women with PCOS with metabolic abnormalities especially diabetes (7, 8). Besides inducing significant weight loss, the surgery also leads to the restoration of hypothalamic-pituitary axis, normal menstruation, and improvement of hirsutism, reduction of the risk of cardiovascular diseases (CVD), improved fertility, and pregnancy outcome (9). However, bariatric surgery is still recommended with low priority in weight loss interventions for patients with obesity and PCOS (10). To address this issue, we conducted a prospective study of women with obesity and PCOS.

## Materials and Methods

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.REC.1402.192). Fifty women between the age group of 18 and 45 years, with morbid obesity defined as  $BMI \geq 40$  kg/m<sup>2</sup> or  $BMI \geq 35$  kg/m<sup>2</sup> with co-morbidities, who were planned for bariatric surgery at our institute were screened using the Rotterdam 2003 criteria for PCOS (11). According to the Rotterdam criteria, the presence of oligo-ovulation or anovulation is essential for diagnosis. PCOS is defined as more than 12 follicles sized 2-9 mm in either or both ovaries, or an ovarian volume  $\geq 10$  mL in either ovary (ovarian volume is calculated as  $0.5 \times \text{ovarian length} \times \text{ovarian width} \times \text{ovarian height}$ ), as determined by ultrasound detection. Patients less than 18 years or more than 40 years of age, with known hypothalamic-pituitary and genetic causes of obesity, and refusing consent were excluded from the study.

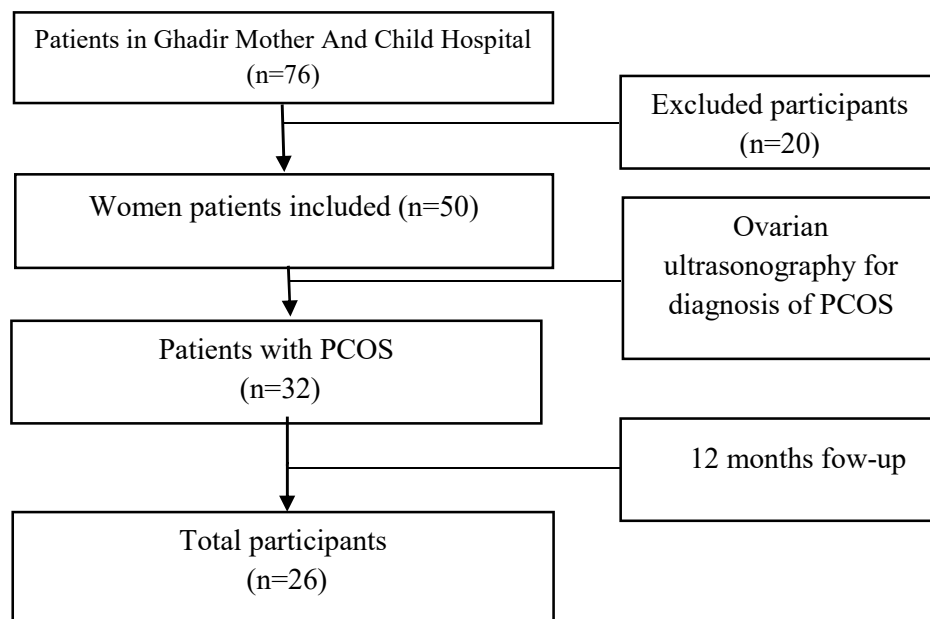
This study was a prospective observational one at a tertiary care center. All subjects were recruited at Ghadir Mother and Child Hospital Affiliated Shiraz University of Medical Sciences, Shiraz, Iran from November 2021 to June 2022. Roux-en-Y gastric bypass (RYGB) was conducted for all patients. Preoperatively, anthropometric data including body weight, height, waist and hip circumferences were assessed. Body weight and height were measured, while the subjects were barefoot and only wearing light clothing. BMI was defined as weight (kg) divided by the squared body height (m<sup>2</sup>). Waist and hip circumferences were measured to calculate the waist to hip circumferences ratio (WC/HC). Baseline

blood samples, including fasting and postprandial samples, were collected randomly for amenorrheic subjects, or during days 3 to 5 of a spontaneous menstrual cycle. Serum levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), total testosterone, fasting plasma glucose (FPG), triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels were determined. Ovarian ultrasonography was conducted by scanning the pelvis using an 8 MHz transducer. Each ultrasonographic detection was performed by a radiologist who was blind to the intervention. Moreover, patients were assessed for clinical signs of hyperandrogenism like acne and hirsutism. Detailed menstrual history was taken including dysmenorrheal and irregular menstruation. Subsequent data was collected at follow-up visits conducted at 1 year following surgery. The primary outcome of the study was to assess the impact of bariatric surgery on PCOS in terms of symptoms and hormonal and radiological profile. Secondary outcomes were to study the prevalence of PCOS, impact of weight loss on improvement of cardiometabolic parameters.

Data were analyzed using SPSS software (Version 23.0, IBM® Corp, Chicago, IL, USA). All data were expressed as the mean  $\pm$  standard deviation (SD) or as numbers and proportions. Descriptive and inferential statistical analyses were performed using both parametric and nonparametric procedures as appropriate. Comparisons of categorical/ordinal variables were performed using Fisher exact test or the Chi-Square test for trends. Continuous variables were compared using an independent t-test or Man-Whitney as appropriate. All tests were two-tailed, and the results with  $p < 0.05$  were considered statistically significant.

## Results

From 50 patients, thirty two (64%) women were diagnosed to have PCOS, which 18 of them (56%) had irregular cycle's pre-operatively (Figure 1). All of them underwent laparoscopic RYGB. The mean postoperative stay was  $1.2 \pm 0.8$  days. There were no intraoperative or postoperative complications. As shown in Table 1, the mean age of the women with PCOS was  $31.27 \pm 3.76$  years (18-40 years). The mean BMI was  $42.38 \pm 4.38$  kg/m<sup>2</sup>. Six women (18.7%) had reported an earlier treatment for PCOS, but had stopped for more than 3 months prior to the surgery. Ten (31.2%) subjects had experienced primary infertility. Preoperatively, 16 women (50%) showed hirsutism. Preoperatively, their mean FSH was  $5.6 \pm 2.35$  mIU/mL and LH was  $8.5 \pm 3.36$  mIU/mL. The mean LH/FSH ratio was 1.51 (Tables 2).



**Figure 1:** Flow chart of participant selection.

**Table 1:** Diagnosis of 32 women with polycystic ovary syndrome candidate for bariatric surgery.

Variable	PCOS women (n=32)
Age (years)	31.27 (3.76)
Weight (kg)	106.1 (10.5)
BMI (kg/m <sup>2</sup> )	42.38 (4.31)
Hip (cm)	115.0 (10.1)
Waist/hip	0.99 (0.06)
Irregular menses, no (%)	18 (75%)
Infertility, no (%)	10 (41%)
Hirsuteism, no (%)	10 (41%)

BMI: Body mass index. Mean (SD) for quantitative and frequency (%) for qualitative variables.

**Table 2:** The changes of study parameters with 1 year follow-up.

Variable	Preoperatively (N=32)	One year post-operatively (N=26)	P value
Weight (kg)	106.1 (10.5)	69 (11.0)	<0.001
BMI (kg/m <sup>2</sup> )	42.38 (4.31)	27.05 (4.11)	<0.001
Waist (cm)	114.2 (8.7)	84 (7.5)	<0.001
Hip (cm)	115.0 (10.1)	94 (6.6)	<0.001
Waist/hip	0.99 (0.06)	0.89 (0.05)	<0.001
FSH (maul/mL)	5.6 (2.35)	5.9 (5.11)	NS
LH (mIU/mL)	8.5 (3.36)	5.02 (2.40)	0.01
LH/FSH ratio (%)	1.51 (0.6)	1.1 (0.4)	0.007
Total testosterone (ng/mL)	2.1 (0.2)	0.9 (0.1)	<0.001
PRL (ng/mL)	9.5 (4.1)	9.9 (4.8)	NS
Hirsutism score	10	4	<0.001
FPG (mg/dL)	108.8 (12.2)	79.2 (8.8)	<0.001
2 h	149.35 (69.95)	117.5 (10.3)	<0.001
Triglycerides (mmol/L)	142.4 (10.7)	85.5 (10.1)	<0.001
Total cholesterol (mmol/L)	200.1 (15.1)	170.5(11.3)	0.011
HDL-C (mmol/L)	45.2 (5.4)	51.3 (4.1)	<0.001
LDL-C (mmol/L)	117 (10.1)	101.3 (6.8)	<0.001

BMI: Body mass index; FSH: Follicle stimulating hormone; LH: Luteinizing hormone; PRL: Prolactin; FPG: Fasting plasma glucose; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol, Mean (SD) for quantitative and frequency (%) for qualitative variables using pair-t-test or Chi-Square.

All of the women had hyperandrogenism with a mean serum testosterone level of  $2.1 \pm 0.2$  ng/mL.

As shown in Table 2, PCOS women had a mean weight loss of  $37 \pm 10$  kg at 1 year which was statistically significant ( $p < 0.01$ ). Besides, the BMI level, decreased from  $42.08 \pm 4.31$  kg/m<sup>2</sup> to  $27.05 \pm 4.11$  kg/m<sup>2</sup> ( $p < 0.001$ ). A significant decrease was also observed in WC and WC/zhc ratio from  $114.2 \pm 8.7$  to  $84.0 \pm 7.5$  cm and  $0.99 \pm 0.06$  to  $0.89 \pm 0.05$ , respectively ( $p < 0.001$ ). All PCOS women with irregular menses restored their normal menstrual cycle at 1 year post-surgery ( $p < 0.05$ ). Among 16 women who had hirsutism preoperatively, 11 women (68.7%) demonstrated resolution of hirsutism at the end of at 1 year post-surgery. Patients had maximum fall in the mean serum testosterone at the end of 1-year follow-up from  $2.1 \pm 0.2$  ng/mL preoperatively to  $0.9 \pm 0.1$  ng/mL ( $p < 0.001$ ). Patients illustrated a significant decrease in the serum level of LH hormone post-surgery and mean LH/FSH ratio significantly decreased from  $1.51 \pm 0.5$  mIU/mL prior to surgery to  $1.1 \pm 0.4$  mIU/mL at 1 year follow-up. Table 2 demonstrates cardiometabolic parameters preoperatively and 1 year after the operation in women with PCOS. Fasting plasma glucose (FPG) and blood sugar at 2 hours after eating (2 h) decreases, postoperatively ( $p < 0.001$ ). Moreover, lipid profiles including TG, total cholesterol, HDL-C, and LDL-C levels improved after the surgery ( $p < 0.01$ ).

## Discussion

We conducted a retrospective observational study to evaluate how bariatric surgery affects the endocrine-metabolic profiles and anthropometric indices of women with obesity and PCOS. According to the present study, bariatric surgery resulted into a significant weight loss with consequent improvements in some markers such as lipid profiles, FPG, testosterone levels, and hirsutism scores. In addition, all women with PCOS regained their regular menstrual cycle after one year of surgery. This finding may provide additional insight regarding the metabolic consequences of bariatric surgery that are independent of weight loss. Consistent with our findings, previous studies have established that bariatric surgery restored menstrual cycle regularity and also improved weight and hirsutism (12-15).

Women who were obese (BMI  $\geq 30$  kg/m<sup>2</sup>) had twice the likelihood of experiencing an irregular menstrual cycle compared to women with normal weight (16, 17). This can be attributed to the fact that obesity leads to an increase in insulin resistance, resulting in elevated production of androgens from thecal cells through LH mediation. Extra gonadal

aromatization of androgens to estrogens leads to a further decrease in FSH and a positive feedback on LH. Therefore, the LH/FSH ratio is altered, leading to anovulation. Anovulation is a significant factor behind irregular menstrual cycles and induces alterations in the ovarian morphology in the form of PCOS (18). According to Casals and colleagues (19), significant weight loss was achieved in all women, and the percentage of women with regular menstrual cycles increased from 52.9% before bariatric surgery to 72.9% in one year. Nevertheless, there is ongoing discussion regarding the amount of weight loss required to restore a regular menstrual cycle. In the present study, we discovered that women with PCOS experienced a notable reduction in weight after undergoing surgery, with an average weight loss of  $37 \pm 10$  kg after one year.

Hirsutism is often more severe in PCOS women with obesity, particularly those with abdominal obesity (20). Hence, weight loss might be effective in this regard. In line with the present study, Bhandari *et al.* (21) conducted a study which showed that out of 993 patients who had hirsutism prior to bariatric surgery, 741 patients (74.6%;  $p < 0.001$ ) experienced complete resolution of hirsutism after 6 months of follow-up. On the contrary, Walędziak *et al.* observed no improvement in hirsutism before and after bariatric surgery (22).

Obesity is also linked to increased testosterone levels in females with PCOS. Indeed, obesity may have the ability to worsen the androgen balance, and this could be linked to insulin resistance and hyperinsulinemia. These conditions may directly contribute to an increase in ovarian steroidogenesis (20). Adipose tissue is also an important site for storing and metabolizing steroid hormones, specifically androgens. Therefore, it is possible that weight loss could have a beneficial impact on reducing testosterone levels (23). The findings of this research confirm earlier studies that have demonstrated a decline in the levels of testosterone following the bariatric surgery (18, 24). Escobar *et al.* also observed a remarkable decline in hirsutism score from 9.5 to 4.9 and mean testosterone level from  $0.69 \pm 0.32$  to  $0.42 \pm 0.19$  ng/mL at the end of 12 months after bariatric surgery (13).

Recently Hu *et al.* carried out a study to evaluate the impact of initial pharmacologic treatment and bariatric surgical treatment on the endocrine-metabolic profiles and clinical symptoms in women who had obesity and PCOS. In their study, it was interestingly discovered that surgical treatment was significantly more effective compared to drug therapy. The researchers observed that bariatric surgery offered various advantages for

PCOS, such as consistent and dependable weight reduction, restoration of irregular menstrual cycles, and improvement in both hormonal and metabolic profiles (25). Furthermore, previous authors have used sex steroids and gonadotropins as indicators before and after bariatric surgery in people with PCOS; however, no significant changes in LH/FSH ratios were detected in this study (26). The main limitation of our study was the restricted number of participants and the fact that we included only one racial or ethnic group, which were also limitation of our study.

### Conclusion

In conclusion, obese PCOS patients were shown to achieve effective and permanent weight loss through bariatric surgery. Furthermore, bariatric surgery was linked to a significant decreases in testosterone level, hirsutism, fasting plasma glucose, and lipid profiles, along with the resolution of irregular menstrual cycles. Thus, bariatric surgery could be an option for women suffering from PCOS who are not achieving adequate weight loss and metabolic improvement with medication alone.

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### Conflict of Interest

The authors declare no conflict of interest.

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