



# Impact of Bariatric Surgery on Clinical, Biochemical, and Hormonal Parameters in Women with Polycystic Ovary Syndrome (PCOS)

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## Abstract

There is limited data on the impact of bariatric surgery on polycystic ovarian syndrome (PCOS) especially in the Indian population. **Background** To study the impact of bariatric surgery in women with PCOS in terms of clinical, hormonal, and radiological aspects of polycystic ovarian syndrome.

**Methods** A prospective observational study of 50 women who underwent bariatric surgery at our tertiary care center. Evaluation of anthropometric data and menstrual cyclicity as well as markers of hyperandrogenism was done preoperatively and at 3- and 6-month and 1-year follow-up.

**Results** Eighteen (36%) women were diagnosed to have PCOS. % EWL at 3-months ( $n = 14$ ), 6-month ( $n = 14$ ), and 1-year ( $n = 11$ ) follow-up was 31%, 49%, and 63% respectively among women with PCOS. All females regained their normal menstrual cycle at 3 months of follow-up. Hirsutism resolved completely among 44% (5/11) with a decline in median hirsutism score from 11 to 9 at 1-year follow-up. Mean serum testosterone decreased from  $0.83 \pm 0.38$  ng/ml preoperatively to  $0.421 \pm 0.25$  ng/ml at 1-year follow-up ( $p < 0.01$ ), whereas changes in levels of serum LH and FSH were not significant. Seventy-seven percent of females (14/18) had polycystic ovaries preoperatively on USG; out of which, 55% (i.e., 4/7) showed complete resolution at 1-year follow-up. Metabolic syndrome resolved completely at 1-year follow-up in both PCOS and non PCOS group.

**Conclusions** Bariatric surgery results in an effective and sustained weight loss with improvement in clinical, hormonal, and radiological parameters associated with PCOS.

**Keywords** Bariatric surgery · PCOS · Polycystic ovaries

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## Introduction

Polycystic ovary syndrome (PCOS) is a common endocrinopathy of adolescents and reproductive age group females with a prevalence ranging from 5 to 18% [1]. It is characterized by oligomenorrhea, clinical signs of hyperandrogenism such as hirsutism, temporal balding, infertility, psychological symptoms such as anxiety, depression, metabolic syndrome features such as dyslipidemia, diabetes, increased cardiovascular disorders, and increased risk of ovarian and endometrial cancer [2]. PCOS refers to a female subtype of metabolic syndrome known as syndrome XX and is characterized by metabolic syndrome in addition to hyperandrogenemia and anovulation in a premenopausal female [3]. Exact etiology of PCOS is still unknown, and the proposed mechanism includes insulin resistance leading to hyperinsulinemia which stimulates ovarian thecal cells for androgen production. The incidence of PCOS in obese women ranges up to 50% [4]. Obesity accounts for the increased insulin resistance in these patients and also contributes to a high

occurrence of metabolic syndrome [5]. Treatment options for PCOS include lifestyle modification, oral contraceptive pills, anti-androgens, and insulin sensitizers. However, most of them are not efficacious. For the obese subgroup of PCOS women, the use of metformin is ineffective, as it does not work beyond a BMI of 35 kg/m<sup>2</sup>. Also, dieting is ineffective in subjects with BMI > 30 kg/m<sup>2</sup>. Exercise and lifestyle modifications also have a high failure rate. Drug therapy can lead to side effects, and the weight loss achieved is modest.

Bariatric surgery is a highly effective treatment option for obese women with PCOS with metabolic abnormalities especially diabetes [6]. Besides inducing significant weight loss, the surgery also leads to the restoration of hypothalamic-pituitary axis, normal menstruation, improvement of hirsutism, reduction of cardiovascular risk, improved fertility, and pregnancy outcome [7].

There have been few studies evaluating the impact of bariatric surgery on PCOS in the Asian population. Hence, we conducted a prospective study to see the impact of bariatric surgery on PCOS women in terms of clinical, hormonal, and radiological aspects of the polycystic ovarian syndrome with a focus on metabolic improvements.

## Methodology

This was a prospective observational study at our tertiary care center. Fifty women between the age group of 18–45 years who were planned for bariatric surgery at our institute were screened using the Rotterdam 2003 criteria for PCOS [8]. Pre operatively in addition to thorough history and general examination, patients were assessed for clinical signs of hyperandrogenism like coarse hair, excessive growth of hair at abnormal sites, acne, and deepening of voice by a dedicated team of dermatologist. Hirsutism was assessed by the Ferriman-Gallwey score [9]. Detailed menstrual history was taken including age at menarche, days of menstruation, length of the menstrual cycle, amount of menstrual blood loss, and dysmenorrhea. Reproductive history like the number of pregnancies, live issues, abortions, use of oral contraceptives, and any prior treatment taken for infertility was taken. Ultrasound pelvis was done to check for any signs of polycystic ovaries or any adnexal mass. Laboratory values depicting markers of metabolic disease like HbA1c, fasting glucose, triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein-C (HDL-C), and markers of hyperandrogenism like total testosterone and free testosterone were recorded in addition to routine blood investigation and hormonal profiles. Subsequent data was collected at follow-up visits conducted at 3 months, 6 months, and 1 year following surgery. Patients underwent bariatric surgical procedure using a standardized technique. 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 metabolic syndrome, and other comorbidities. Patients with body mass index (BMI)  $\geq$  40 kg/m<sup>2</sup> or BMI  $\geq$  35 kg/m<sup>2</sup> with comorbidities and diagnosed to have PCOS (Rotterdam Criteria) were included. 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.

## Statistics Analysis

Continuous variables were expressed as mean  $\pm$  standard deviation or median (with interquartile range) as appropriate. Preoperative and postoperative results of nominal values were compared using the McNemar test. Ordinal values were compared using the Wilcoxon signed rank test. The results of parametric variables were compared using the paired *t* test. Pearson correlation coefficient was used to identify predictors of change in parameters of PCOS post-surgery. Statistical significance was considered as *p* value less than 0.05. Statistical analysis was done using SPSS 20.0 statistical software.

## Results

Eighteen (36%) women were diagnosed to have PCOS, and an additional 8 women (16%) had irregular cycles pre operatively. Sixty-six percent (12/18) of them underwent laparoscopic sleeve gastrectomy, while 27% (5/18) underwent laparoscopic gastric bypass and 5% (1/18) underwent mini gastric bypass/one anastomosis gastric bypass. The mean postoperative stay was 3.6  $\pm$  0.8 days. There were no intraoperative or postoperative complications. The median follow-up period was 12 months (3–12 months). Among them, 14 patients (14/15, i.e., 93%) had completed 3- and 6-month follow-up while 11 (11/15, i.e., 73.3%) had completed 1-year follow-up. One patient was lost to follow-up during the entire study period, and three patients were lost to follow-up at 6 months.

## Demographic and Baseline Characteristics

As shown in Table 1, the mean age of the women with PCOS was 29.7  $\pm$  5.9 years (18–40 years). The mean BMI was 44.9  $\pm$  7.5 kg/m<sup>2</sup> (29–60). All the women had irregular cycles preoperatively. Eleven of them (61%) had treatment earlier for PCOS but had stopped for more than 2 months prior to surgery. Four (22%) among them had primary infertility. Preoperatively, 16 women (88%) had hirsutism. Their median Ferriman-Gallwey score of hirsutism was 11, and none of them had acne. All of the women had hyperandrogenism biochemically with a mean serum

**Table 1** Baseline characteristics

Characteristic	PCOS women ( <i>n</i> = 18)	Irregular cycle non PCOS women ( <i>n</i> = 8)	<i>p</i> value
Mean age (years)	29.7 ± 5.9	28 ± 6.1	0.5
Mean weight (kg)	112.6 ± 16	118 ± 19.9	0.46
Mean BMI (kg/m <sup>2</sup> )	44.9 ± 7.5	47.8 ± 6.5	0.35
Mean FSH (mIU/ml)	5.9 ± 2.3	6.3 ± 4.1	0.75
Mean LH (mIU/ml)	9.5 ± 4.5	8.5 ± 4.3	0.60
Mean LH/FSH ratio	1.6	1.3	0.51
Mean serum testosterone (ng/ml)	0.8 ± 0.4	0.4 ± 0.09	0.01
Median hirsutism score	11	2	< 0.001
Metabolic syndrome	8	4	NA

PCOS, polycystic ovarian syndrome

testosterone level of  $0.83 \pm 0.4$  ng/ml. Their mean FSH was  $5.9 \pm 2.3$  mIU/ml and LH was  $9.5 \pm 4.5$  mIU/ml. The mean LH/FSH ratio was 1.6 (Tables 2 and 3).

Further, the weight loss was correlated with the change in hormones over a follow-up of 1 year. The Spearman correlation coefficients between weight loss and change in serum FSH and LH were found to be 0.219 and 0.279 respectively. However, the results were not statistically significant. Similarly, the Spearman correlation coefficients between weight loss and change in serum testosterone and change in hirsutism score were 0.384 and 0.252 respectively (*p* value > 0.05).

Metabolic syndrome was identified in eight women. Four (25%) women were associated with type 2 diabetes mellitus with the requirement of insulin for control of blood sugars, and four women had hypertension preoperatively.

The non PCOS women with irregular cycles had a mean FSH of  $6.3 \pm 4.1$  mIU/ml, LH of  $8.5 \pm 4.3$  mIU/ml, and serum testosterone of  $0.4 \pm 0.09$  ng/ml with normal ovaries. Metabolic syndrome was seen in four (50%) women.

## Follow-up of PCOS Women

**Impact of Bariatric Surgery on Weight** As shown in Fig. 1, PCOS women had a mean weight loss of  $25 \pm 8$  kg at 6 months of follow-up and  $34 \pm 11$  kg at 1 year which was significant (*p* < 0.01). Their mean excess weight loss (% EWL) at

3 months (*n* = 14) was  $31\% \pm 13.88$ , at 6 months (*n* = 14) was  $49\% \pm 10.62$ , and at 1 year (*n* = 11) was  $63\% \pm 7.91$ .

**Impact of Bariatric Surgery on Menstrual Cycle** All PCOS women restored their normal menstrual cycle at 3 months post-surgery and continued to have normal menstrual pattern during the entire follow-up period of 1 year (*p* < 0.05).

**Impact of Surgery on Hirsutism** Among 16 women who had hirsutism preoperatively, 4 women (30%, i.e., 4/13) had resolution of hirsutism at the end of 6 months and additionally one woman (44%, i.e., 5/11) had resolution at the end of 1 year post-surgery. Patients had a decrease in median hirsutism score from 11 to 8.5 at 6 months (*p* < 0.04) which was significant and then maintained at 9 after 1 year post-surgery.

**Impact of Surgery on Hormones** Patients had maximum fall in the mean serum testosterone at the end of 3 months from  $0.8 \pm 0.4$  ng/ml preoperatively to  $0.5 \pm 0.3$  ng/ml (*p* < 0.05) at the end of 3 months and then a sustained decrease to a mean of  $0.4 \pm 0.3$  ng/ml at 6 months (*p* < 0.05) and a mean of  $0.4 \pm 0.2$  ng/ml at 1-year follow-up (*p* < 0.01).

Patients had a variable change in the serum FSH and LH hormones post-surgery and mean LH/FSH ratio which was elevated to  $1.6 \pm 0.5$  prior to surgery had decreased to  $1.2 \pm 0.6$  at 6 months and  $1.3 \pm 0.6$  at 1 year which was not significant.

**Table 2** Change in the clinical, hormonal, and radiological parameters after bariatric surgery

Change in parameters	Pre surgery	3 months	6 months	12 months
Excess weight loss percent	0	31%*	49%*	63%*
Hirsutism (Ferriman-Gallwey score)	11	10*	8.5*	9*
Serum testosterone (ng/ml)	$0.8 \pm 0.4$	$0.5 \pm 0.3^*$	$0.4 \pm 0.3^*$	$0.4 \pm 0.2^*$
LH/FSH ratio	$1.6 \pm 0.5$	$1.6 \pm 0.5$	$1.2 \pm 0.6$	$1.3 \pm 0.6$
Polycystic ovaries (ultrasound)	<i>n</i> = 14/18	<i>n</i> = 8/10	<i>n</i> = 7/10	<i>n</i> = 3/7

*p* value < 0.05

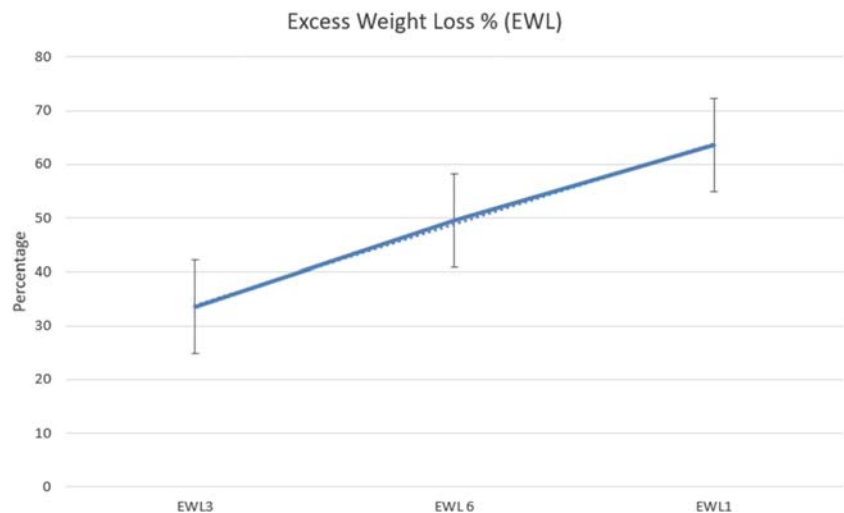
LH, luteinizing hormone; FSH, follicles-stimulating hormone

**Table 3** Various studies showing impact of bariatric surgeries on menstruation, hirsutism and hormonal profile in women with Polycystic ovarian syndrome

Characteristic	Eid et al. [10] (N= 14), retrospective	Escobar et al. [11] (N= 12), retrospective	Jamal et al. [7] (N= 20), retrospective	Eid et al. [12] (N= 24), retrospective	Christ [13] (N= 44), retrospective	Turkmen [14] (N= 13), prospective	Our study (N= 18), prospective
Baseline weight in kg	110 ± 3.6	114 ± 15	147 ± 4.08	138.8 ± 19.9	121.8 ± 5.5		112.6 ± 16
Weight loss at 6 months	37 ± 11		45 ± 6				25 ± 8
Weight loss at 1 year	45 ± 13	41 ± 9	50 ± 7		93.6 ± 3.5		34 ± 11
% excess weight loss 1 year	66.5%		50%	56.7%			63%
Menstrual cycles baseline	10/14 irregular (72%)	12/12 irregular (100%)	18/20 irregular (90%)	24/24 irregular (100%)	37/44 (83% irregular)	13/13 (100%)	18/18 irregular (100%)
Menstrual cycle 6 month		100% regular	66.6% regular	100% regular		7/13 (53.8%)	100% regular
Menstrual cycle 1 year		100% regular	90% regular	100% regular	8/44 irregular (17%)		100% regular
Hirsutism baseline	78%		70%	96% (23/24)			88% (16/18)
Hirsutism 6 months	–	–	45%	52% (12/23)			62% (10/14)
Hirsutism 1 year	50%	–	40%	78% (18/23)			55% (6/11)
Testosterone baseline (ng/dl)	59 ± 2*	69 ± 32*	–	–	63	53.3	83 ± 38*
Testosterone 6 months (ng/dl)	31 ± 4.1*		–	–		32.3	49 ± 27*
Testosterone 1 year (ng/dl)	23 ± 12.5*	42 ± 19*	–		34.6		42 ± 25*
Mean follow up (months)	12	12 ± 5	46	27.5 ± 16	22.8 ± 3.6	6	12

\*Statistically significant ( $p < .05$ )

**Fig. 1** %Excess Weight Loss post-surgery in women with polycystic ovarian syndrome



**Impact of Bariatric Surgery on Ovarian Morphology** Initially, 14/18 PCOS women (i.e., 77%) had polycystic ovaries on USG. There was a gradual reduction in terms of the number of follicles and decrease in ovarian volume in all women except in one woman who had similar ovarian characteristics in the entire follow-up period. The reduction in ovarian morphology was gradual and sustained in the entire follow-up. There was complete resolution in 2 (20%, i.e., 2/10) women at the end of 3 months with additional 1 woman (30%, i.e., 3/10) at the end of 6 months and in 4 women (55%, i.e., 4/7) at the end of 1-year follow-up.

**Impact of Surgery on Metabolic Syndrome and Comorbidities** Metabolic syndrome resolved among 3 patients (60%, i.e., 3/5) at 3 months, additionally in one woman (80%, i.e., 4/5) at 6 months, and in all of them (100%, i.e., 5/5) at 1-year follow-up.

**Non PCOS Women** Among the women who had irregular cycles but not diagnosed as PCOS, 78% (6/8) had regular cycles at 3 months post-surgery while 100% (6/6) had regular cycles at 6 months and 1 year post-surgery. There was a decrease in mean serum FSH from  $6.3 \pm 4.1$  mIU/ml pre-operatively to  $4.2 \pm 2.3$  mIU/ml at 1 year and LH from  $8.4 \pm 4.3$  mIU/ml preoperatively to  $3.2 \pm 1.6$  mIU/ml at 1 year. There was also a decrease in serum testosterone from  $0.4 \pm 0.07$  ng/ml preoperatively to  $0.3 \pm 0.07$  ng/ml at the end of 1-year follow-up. Metabolic syndrome resolved among all women at 3 months and continued until 1-year follow-up period.

## Discussion

In our study, 18/50 (i.e., 36%) premenopausal morbidly obese women who underwent bariatric surgery were diagnosed to have PCOS and an additional 8 women (16%) had irregular cycles preoperatively. Metabolic syndrome was seen in 46% of them (8 in PCOS and 4 in non PCOS with irregular menses

group). Bariatric surgery resulted in the improvement of all parameters of PCOS with complete resolution of abnormal menstruation and metabolic syndrome at 1-year follow-up. Hirsutism and polycystic ovarian morphology on ultrasonography resolved in 44% and 55% respectively.

The meta-analysis done by Skubleny [15] in 2016 found the incidence of PCOS to be 45.6% among the premenopausal women. Escobar et al. [16] had found PCOS in 47% of the premenopausal women who underwent bariatric surgery. They reported irregular menstrual cycle in all PCOS women who underwent bariatric surgery and found biochemical hyperandrogenism with mean serum testosterone of  $0.7 \pm .3$  ng/ml and hirsutism score of  $8.1 \pm 6$  which were similar to our study. Metabolic syndrome has been reported in 46% of PCOS women [11].

The above findings can be explained by an obesity-associated increase in insulin resistance which causes increase LH-mediated androgen production from thecal cells. Extra gonadal aromatization of androgens to estrogens leads to a further decrease in FSH and positive feedback on LH. Hence, there is a change in LH/FSH ratio causing anovulation. Anovulation is a major cause of the irregular menstrual cycles and causes a change in the ovarian morphology in the form of polycystic ovarian disease [17].

Teitelman et al. [18] reported that all women achieved significant weight loss and 70% restored regular menstrual cycles at the end of 1 year. The minimum amount of weight loss required for the restoration of regular cycles is still debated. In our study, we have found that PCOS women have achieved a significant weight loss post-surgery achieving up to 63% EWL at the end of 1 year. All the PCOS women had restoration of regular menstrual cycles at 3 months post-surgery with 31% EWL and maintained it during the entire follow-up period of 1 year. In non PCOS women with irregular menstrual cycles, restoration of regular cycles was seen in 75% (6/8) at 3 months and 100% at 6 months and 1 year post-surgery (6/6). However, further studies are required to evaluate the minimum weight loss required for the restoration of menstrual cycles.



In our study, women with PCOS showed significant resolution of hyperandrogenism post-surgery. Hirsutism was resolved in 4 women at the end of 6 months (4/13) and in another woman at the end of 1 year (5/11). They had a decrease in median FG score from 11 preoperatively to 8.5 at 6 months ( $p < 0.04$ ) which stabilized at 9 at 1 year. The disparity between the results of 6 months and 1 year post-surgery seems to be because of loss to follow-up of those women who had better response. Escobar also reported a significant decrease in hirsutism score from 9.5 to 4.9 and mean testosterone from  $0.69 \pm 0.32$  to  $0.42 \pm 0.19$  ng/ml at the end of 12 months following bariatric surgery. In our study, we found a positive correlation between weight loss at 6 months and decrease in serum testosterone at 1 year ( $p < 0.05$ ). The effect of bariatric surgery on hyperandrogenism can be explained by the decrease in insulin resistance, adipokines, and inflammatory mediators (IL-6, TNF- $\alpha$ ) which causes a decrease in LH-mediated androgen secretion and reduced peripheral aromatization [19].

Our study showed an improvement in ovarian morphology in all except one woman (13/14) with PCOS. These results could be explained by the improvement in hormone profile which causes an improvement in the ovulatory pattern. However, only four out of seven (55%) had complete resolution post-surgery. These results are consistent with the retrospective analysis done by Christ et al. [20] who found a decrease in postoperative volume from  $14 \pm 9.8$  to  $7.7 \pm 4.8$  ml postoperatively over 6 years ( $p < 0.05$ ). The impact of bariatric surgery on the resolution of polycystic ovaries on ultrasound is limited compared with its impact on menstrual irregularities and hyperandrogenism as seen by Christ et al. They also noted that the impact on ovarian morphology is more pronounced in women with PCOS compared with non PCOS women.

Resolution of metabolic syndrome was seen in among 4 patients at the end of 6 months (80%, i.e., 4/5) and among all of them (100%) at end of 1-year follow-up, and resolution of diabetes was seen in all of the 4 women post-surgery, similar to Jamal et al. [7] who found resolution of diabetes in 78% (7/9) among PCOS women. The above findings can be explained by the increased gastric emptying post bariatric surgery which further leads to GLP-1-mediated insulin secretion and the associated

decrease in ghrelin and leptin which increase the serum insulin and decrease the insulin resistance [21].

Strength of our study is that it is one of the few studies regarding the effect of bariatric surgery with PCOS as a primary end point. To our knowledge, this study is the first of its kind to be done in the Indian population with PCOS as the primary end point. There are few limitations to our study. Our study had small sample size, and follow-up of all patients could not be completed. The long-term effect on reproductive parameters such as infertility could not be assessed.

### Conclusion

PCOS is commonly associated with morbid obesity in premenopausal women. Bariatric surgery results in an effective and sustained weight loss with improvement in the clinical, hormonal, and radiological parameters associated with PCOS. Further studies with long-term follow-up are needed to identify the role of bariatric surgery in class one obese premenopausal woman with PCOS.

### Compliance with Ethical Standards

The study was undertaken after clearance from the institutional ethical committee. There was no commission or omission of intervention for the study purpose, and all the interventions were done in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Written informed consent was taken from each patient for the surgical procedure.

**Conflict of Interest** The authors declare that they have no conflict of interest.

### Contribution Details (to be ticked marked as applicable):

	Devender Singh	Kirit Arumalla	Sandeep Aggarwal	Vitish Singla	Ashraf Ganie	Neena Malhotra
Concept	✓		✓			
Design	✓	✓	✓			
Definition of content	✓	✓	✓			
Literature search	✓	✓		✓		
Clinical studies	✓	✓	✓			
Data and statistical analysis	✓	✓		✓	✓	
Data acquisition	✓	✓		✓	✓	✓
Manuscript preparation	✓	✓		✓	✓	
Manuscript editing	✓	✓				
Manuscript review	✓	✓	✓	✓	✓	✓
Guarantor	✓		✓			

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