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The impact of bariatric surgery on obesity-related infertility

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Abstract. – OBJECTIVE: **Our study aimed to investigate the effect of morbid obesity surgery on infertility using laparoscopic sleeve gastrectomy (LSG).**

PATIENTS AND METHODS: **We performed a retrospective analysis from a prospectively collected database from May 2014 until December 2019. The mean age of the 23 morbidly obese women included in the study and followed-up for five years was 31.26 ± 5.06 years (minimum 24, maximum 43), mean duration of marriage was 9.3478 ± 4.76 years (minimum 4, maximum 23). Mean body mass index (BMI) values were 45.04 ± 3.43 (minimum 40, maximum 52) pre-LSG and 28.65 ± 3.14 (minimum 24, maximum 36) 12 months post-laparoscopic sleeve gastrectomy (LSG).**

RESULTS: **Out of 23 infertile patients studied underwent LSG. Significant correlation was determined between the change in BMI, 12 months after LSG, compared to pre-LSG and having children after surgery (*p*=0.001). Conception occurred in 21 patients (91.3%) after surgery, but not in the remaining two (8.7%).**

CONCLUSIONS: **LSG is an important surgical technique used in the treatment of obesity and in preventing obesity-related comorbidities. It can improve pregnancy and live birth rates by contributing to weight loss and hormonal regulation in obese infertile women.**

Key Words:

Obesity, Fertility, Laparoscopic sleeve gastrectomy, Bariatric surgery.

Introduction

Infertility is defined as the inability to achieve pregnancy following regular unprotected sexual relations for 12 months or longer[1].

As a factor involved in every stage of pregnancy, obesity makes natural pregnancy difficult, increases the risk of pregnancy-related complications, leads to miscarriages and congenital anomalies, and thus has an adverse effect on the health of both mother and child.

Overweight infertile women have been shown[2] to take longer to conceive, and to exhibit lower rates of spontaneous pregnancy and higher rates of infertility treatment cycle cancellation and failure.

Obesity is characterized by insulin resistance and 'compensatory hyperinsulinemia' associated with several factors, particularly central obesity, free fatty acids (FFAs), leptin, cytokines, and androgens[3]. In case of obesity, muscle, hepatic, and adipose tissue in particular become resistant to insulin, while the ovaries remain insulin-sensitive and thus exposed to the effects of insulin. In the ovaries, insulin stimulates theca cells to produce androgens, both through direct action and also by increasing local sensitivity to luteinizing hormone (LH). Excessive androgen production in the ovaries supports early follicular atresia and anovulation[4]. With all these mechanisms, insulin resistance leads to obesity in women and particularly to central obesity accompanying menstrual, ovulatory, and fertility disorders.

Body fat in women affects the function of the hypothalamus-pituitary-ovarian axis by means of central and peripheral mechanisms[5]. The role of adipocytokines, and particularly leptin, has been widely investigated in literature. Some evidence[6] from cellular and animal models has shown that, due to its stimulating effect on the gonadotropin-releasing hormone (GnRH) pulse, leptin is a major determinant of puberty and future fertility. Ovarian-derived leptin inhibits both granulosa and thecal cell steroidogenesis and interferes with ovulation, thus exerting a direct effect on fertility[7].

The most frequent cause of infertility in women is polycystic ovarian syndrome (PCOS). The estimated prevalence among women of child-bearing

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Table I. Age of patients, duration of marriage and mean postoperative pregnancy period.

	Minimum	Maximum	Mean±Standard Deviation
Mean age (years)	24	43	31.26 ± 5.06
Duration of marriage (years)	4	23	9.3478 ± 4.76
Mean postoperative time to pregnancy (months)	18	35	25.6 ± 4.7

age is greater than 10%[8]. The etiology of PCOS is unknown, although it probably represents a complex combination of environmental and genetic factors. In addition to being associated with infertility, PCOS is also linked to type 2 diabetes mellitus (DM), endometrial carcinoma, stroke, and coronary heart disease. More than 50% of women with PCOS are obese. It has been suggested[9] that even a mild loss of 5% of initial body weight in obese women with PCOS can result in spontaneous ovulation, regularization of the menstrual cycle, and pregnancy.

The British Fertility Society Guidelines[10] recommended postponing fertility treatment until body mass index decreases to lower than 35 kg/m^2 in morbidly obese women, preferably reaching a value lower than 30 kg/m^2 in individuals aged under 37 with normal ovarian reserves.

Bariatric surgery, the most permanent and effective therapy, improves PCOS markers that affect fertility, such as anovulation, hirsutism, hormonal changes, insulin resistance, sexual activity, and libido[11]. The purpose of the present study was to investigate the effect of morbid obesity surgery on infertility using laparoscopic sleeve gastrectomy (LSG).

Patients and Methods

Prospectively collected data from primary infertile, childless, morbidly obese women with BMI values > 40 undergoing LSG between May 2014 and December 2019 at Adıyaman Medical Faculty Training and Research Hospital General Surgery clinic, Turkey, were analyzed retrospectively. Body mass index (BMI) values were calculated as weight/height^2 (kg/m^2). Follicle-stimulating hormone (FSH), LH, estradiol, prolactin, and testosterone levels were measured and recorded before and 12 months after LSG using a Beckman Coulter Unicel Dz1800 device (Brea, CA, USA) and the immunoassay method. Patients screened before LSG in terms of PCOS using ultrasound were divided into two groups: those with and those without PCOS. Hypertension (HT), DM, smoking status, and alcohol consumption habits were determined. No heart failure, kidney failure, peripheral neuropathy, pregnancy, arterial insufficiency, or neurological disease were present in any patient. Women with histories of pregnancy before LSG, pregnant women, individuals with any systemic disease other than diabetes and HT, with secondary infertility, primary ovarian insufficiency, or endometrial pathology were excluded from the study.

Statistical Analysis

To evaluate the assumption of normality in the data, the Kolmogorov-Smirnov test was used; and to describe the data, frequency (percent), mean ± SD, median and quartile were used. Chi-square test was used to analyze qualitative variables. The paired samples *t*-test and Wilcoxon signed ranks test were used to compare pre- and post- operative values of patient-related variables. *p*-value lower than 0.05 was considered as statistically significant. All statistical analyses were performed by SPSS software version 21.0, for Microsoft (IBM Corp., NY, Armonk, USA).

Results

The mean age of the 23 morbidly obese women included in the study and followed-up for five years was 31.26 ± 5.06 years (minimum 24, maximum 43), mean duration of marriage was 9.3478 ± 4.76 years (minimum 4, maximum 23), and mean postoperative time to pregnancy was 25.6 ± 4.7 months (minimum 18, maximum 35) (Table I).

Mean BMI values were 45.04 ± 3.43 (minimum 40, maximum 52) pre-LSG and 28.65 ± 3.14 (minimum 24, maximum 36) 12 months post-LSG (Table II). Patients' BMI values decreased significantly 12 months following LSG compared to preoperative values (p=0.00001) (Table II).

In terms of hormone parameters before and 12 months after LSG, while no significant difference was observed in estradiol and testosterone levels, significant differences were found in LH, prolactin, and FSH values (Table III)

Significant correlation was determined between the change in BMI 12 months after LSG

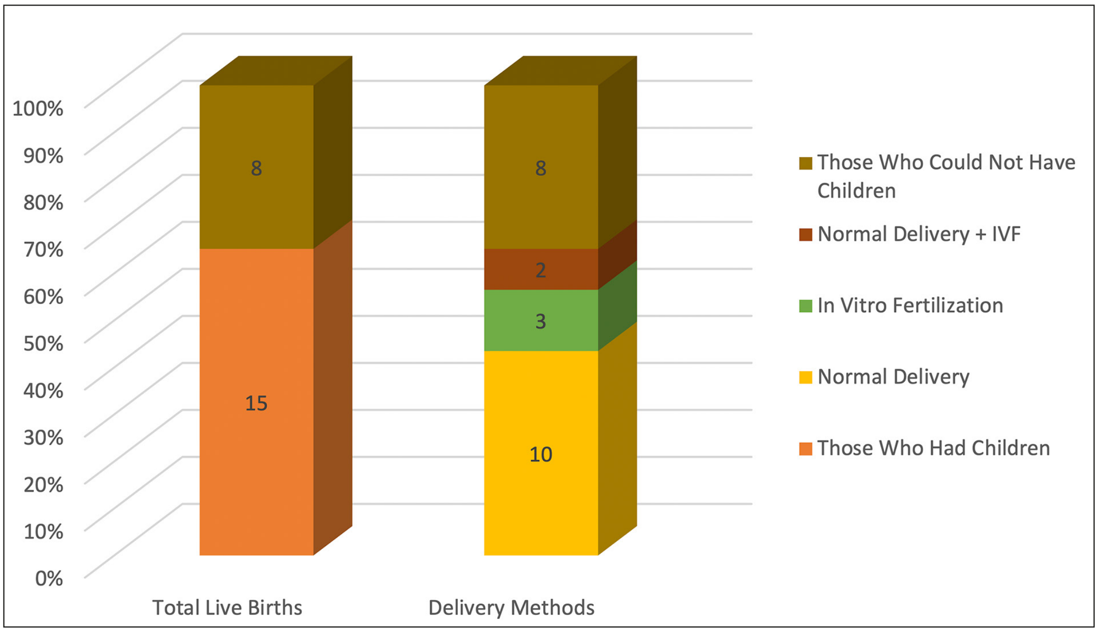

Figure 1. Rates of successful pregnancy in the postoperative period and the methods employed.

compared to pre-LSG and having children after surgery (p=0.001). Conception occurred in 21 patients (91.3%) after surgery, but not in the remaining two (8.7%). Fifteen (71.42%) of the patients in whom conception occurred went on to have children, while abortus developed in the other six (28.58%). The live birth rate in the entire patient group was 65.21%. Nineteen (82.6%) patients were fertile women who had attempted *in vitro* fertilization (IVF) prior to LSG, 11 (57.89%) went on to have children after LSG. Ten patients (66.67%) had children by natural conception (NC) after surgery, two (13.33%) by both NC and IVF, and three (20%) by the IVF method alone. Two of the four patients who had not attempted IVF before surgery became pregnant *via* IVF after surgery (Figure 1).

PCOS was present in 15 (65.2%) of the patients included in this study, all of whom, with one exception, managed to have children after surgery.

Patients' smoking and alcohol consumption habits and accompanying DM, HT, and PCOS are shown in Table IV.

Table II. Patients' pre- and postoperative BMI values.

	Mean±SD
Preoperative BMI	45.04 ± 3.43
Postoperative BMI	28.65 ± 3.14
p-value	p=0.00001

Discussion

In addition to causing several comorbid conditions, obesity is also an important public health problem for women of reproductive age due to its adverse gynecological and obstetric effects during pregnancy. It leads to such gestational complications as gestational diabetes, hypertensive disorders, infertility, stillbirth, and abortus[12].

Increased BMI causes a decrease in fertility rates by contributing to chronic anovulation and subfertility as a result of hyperleptinemia, insulin resistance, and hyperandrogenism[13]. Luke et al[14] reported a 50% decrease in the probability of

Table III. Patients' pre- and postoperative hormone parameters.

	FSH	PRL	LH	Estradiol	Testosterone
Preoperative	7.26 ± 5.46	12.50 ± 6.94	5.57 ± 3.55	31.12 ± 16.68	1.11 ± 0.51
Postoperative	7.74 ± 2. 88	15.20 ± 11.45	8.11 ± 4.50	80.21 ± 40.83	0.44 ± 0.20
p-value	p=0.231	p=0.598	p=0.029	p=0.000	p=0.000

Follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL).

live birth in women with class III obesity (BMI > 40 kg/m^2). Similarly, Kort et al[15] reported significantly higher pregnancy and live birth rates in patients achieving weight loss of ≥ 10% compared to those with weight loss < 10% (pregnancy rates 88% *vs.* 54%, live birth rates 71% *vs.* 37%, and spontaneous conception rates 35% *vs.* 17%, respectively).

BMI values decreased significantly post-LSG compared to pre-LSG values in the present study (p= 0.00001). Significant correlation was determined between postsurgical conception and changes in BMI before and 12 months after LSG (p=0.001). With the decrease in BMI values, the conception rate after surgery was 91.3%, with a live birth rate of 65.2%. Musella et al[16] determined a fertilization and live birth rate of 62.7% in infertile obese women. Those authors[16] reported that although pregnancy rates were higher in patients who underwent LSG, no difference was observed in terms of the surgical procedures' fertilization rates, and they concluded that BMI and postsurgical weight loss were significant determinants of pregnancy.

Christinajoice et al[17] reported a postoperative fertility rate of 43.75% in their 45-patient obesity surgery series in which LSG was performed on 40 women, Marceau et al[18] a fertility rate of 46.9% following bariatric surgery, and Milone et al[19] a fertility rate of 58% following bariatric surgery in their meta-analysis. Deitel et al[20] reported an infertility rate of 25.2% in morbidly obese women of reproductive age undergoing bariatric surgery (29 preoperatively infertile patients), and that nine of the patients enrolled conceived postoperatively.

Nineteen (82.6%) of the patients in the present study consisted of fertile women who had attempted IVF prior to LSG. Eleven (57.89%) of these achieved successful pregnancies after LSG. Every unit increase in BMI has been reported[21] to reduce the possibility of pregnancy with IVF, the risk of miscarriage increasing after IVF, and lower implantation rates have also been reported[2] in obese women. However, a decrease in body weight has been observed[22] to be capable of increasing the success of IVF treatment in terms of pregnancy rates and of numbers of oocytes retrieved and developing. In their meta-analysis, Sermondade et al[23] reported a decreased probability of live birth after IVF in obese women compared to normal weight individuals.

PCOS is also regarded as one of the most important causes of anovulatory infertility in women. Obesity affects approximately half of women with PCOS and increases infertility through its adverse effects on the menstrual cycle, ovulation, pregnancy, and live birth rates[24]. PCOS was present in 15 (65.2%) of the patients included in the present study, all of whom, with one exception, were able to have children after surgery. Our fertility rates in these patients were close to the values reported in some previous studies[25], but higher than those in others. In their cohort study, Edison et al[26] reported a prevalence of PCOS in obese patients of 15.7%, while in their meta-analyses Escobar-Morreale et al[27] reported a figure of 36%, and Jamal et al[25] a prevalence of 5.5%. In one meta-analysis study examining the effect of obesity surgery on fertility in women with PCOS, Skubleny et al[28] reported that the prevalence of infertility decreased from 18.2% to 4.3% one year after bariatric surgery in women with severe obesity and PCOS. Jamal et al[25] reported achieving a 100% conception rate following obesity surgery in pre-surgically infertile women with PCOS.

Obesity directly synthesizes androgens *via* increasing adipose tissue and converts them into estriadols. This results in an increase in both estriadols and androgens[29]. The resulting functional hyperandrogenism also affects ovarian functions and becomes a factor that mediates the development of infertility among obese individuals. While statistically significant differences were determined in our patients' estradiol and testosterone levels among the hormone parameters measured before and 12 months after LSG, no significant difference was observed in LH, prolactin, or FSH levels. Estradiol levels increased in line with weight loss in our patients, while testosterone levels decreased. These findings were similar to those of previous studies[13,30]. Nilsson-Condori et al[3] reported a significant decrease in testosterone and a significant increase in estradiol levels in the postoperative 12th month and reported statistically insignificant decreases in LH and FSH values. Kjær et al[31] determined a significant difference between preoperative testosterone levels and those at 12 months postoperatively, but found no significant difference in FSH, LH, or estradiol values (FSH and LH increased postoperatively, while estradiol decreased).

Limitations

There are a number of limitations to this study. These include the fact that only the bariatric surgical method was employed, that reproductive functions were not investigated over longer periods, our inability to compare the effects of other non-surgical weight loss methods, and the absence of a control group. The lack of a control group was due to the patients included in the study being designed to constitute their own control group.

Conclusions

LSG is an important surgical technique used in the treatment of obesity and in preventing obesity-related comorbidities. It can improve pregnancy and live birth rates by contributing to weight loss and hormonal regulation in obese infertile women. The present study supports the idea that weight loss methods such as LSG are among those that should be promoted due to their fertility-enhancing effects in infertile women. We think that it will be now useful to investigate the effects of weight loss methods together with other variables in the treatment of fertility and for longer follow-ups to be performed.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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Ethics Approval
The study has complied with the principles outlined in the Declaration of Helsinki, and the Local Ethics Committee of the Adiyaman University Faculty of Medicine approved the study protocol (2018/8-33).

Informed Consent
Informed consent was not required due to the retrospective nature of the study.

Authors' Contributions
R.I.O., S.O. were involved in planning and supervised the work. R.I.O., M.S. and S.A. processed the data, performed the analysis, drafted the manuscript and designed the figure. R.I.O. and M.S. aided in interpreting the results and worked on the manuscript. All authors read and approved the final version of the manuscript.

Availability of Data and Materials
The data supporting this article are available from the corresponding author on reasonable request.

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