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ORIGINAL CONTRIBUTIONS

Impact of Bariatric Surgery on Female Reproductive Health and Maternal Outcomes

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Abstract

Introduction Obesity has a derogatory effect on female reproductive health. Obesity contributes to difficulty in natural conception, increased risk of pregnancy-associated complications, miscarriages, congenital anomalies, and also the long-term negative impact on both mother and the child.

Objectives Our study aimed to analyze and assess the reproductive health-associated outcomes of females who underwent bariatric surgery.

Methods We performed a retrospective analysis from a prospectively collected database from June 2013 to June2016. Out of 71 females studied, 45 patients (63.5%) had completed 3 years of follow-up. The data were collected from inpatient and outpatient records. Patients were studied under three groups (A, patients with polycystic ovarian disease (PCOD) symptoms; B, patients with primary infertility; and C, patients who conceived after bariatric surgery that were included in groups A and B).

Results Out of 45 patients studied, 40 patients underwent laparoscopic sleeve gastrectomy (LSG), four patients underwent laparoscopic Roux-en-Y gastric bypass (RYGB), and one patient underwent laparoscopic adjustable gastric banding (LAGB). The mean BMI of the patients was 43.64 ± 6.8 kg/m^2. PCOD symptoms improved symptomatically ($p = 0.001$) after surgery in the group. Seven (43.75%) primary infertility patients conceived after surgery. Three (42.9%) patients conceived naturally while 4 (57.1%) conceived with ART in group B. Out of total population of 45 in group C, percentages of patients who delivered baby with short gestational age (SGA), low birth weight (LBW), normal vaginal deliveries (NVD), and maternal anemia were 63.15%,47.3%,73.4%, and26.3%, respectively.

Conclusion Obesity is closely associated with primary infertility and PCOD. Menstrual abnormalities associated with PCOD significantly improve after bariatric surgery with significant improvement in fertility along with maternal outcomes.

Keywords BS · bariatric surgery · LSG, laparoscopic sleeve gastrectomy · RYGB, Roux-en-Y gastric bypass · PCOD · Small for gestational age · Low birth weight · ART, assisted reproductive technique

Introduction

The global prevalence of obesity has nearly tripled between 1975 and 2016 [1]. Prevalence of overweight and obesity has increased by many-fold among most Asian countries in the past few decades [2, 3]. Literature has shown 39% of men and 40% of women were overweight while two in every five adults were obese [4]. Eleven percent of men and 15% of

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women were obese as estimated by the WHO (BMI > 30 kg/m^2) [1]. Apart from the pathological and psychosocial outcomes, obesity predisposes metabolic disorders like insulin resistance, type 2 diabetes (T2DM), systemic hypertension (SHT), dyslipidemia, obstructive sleep apnea (OSA), PCOD, and related infertility [5].

In a study done by Leddy MA et al. and Fitzsimons et al., it was shown that maternal obesity increased the risk of pre-eclampsia, C-section, stillbirth, and congenital anomalies in obese pregnant females [6, 7]. A balanced diet with restricted calories and physical exercise is the key to weight loss and formed the primary treatment for obesity. Bariatric surgery was considered as the option for BMI > 40 or BMI > 35 with comorbidities like T2DM, SHT, dyslipidemia, OSA, and PCOD [8, 9].

Methods

The study was a single institutional, retrospective study. Data of patients who underwent bariatric surgery between June2013 and June 2016 with an age limit of 14 to 30 years were collected from inpatient case sheet and outpatient follow-up. The remaining information was obtained through telephonic conversations. We performed the study in the Department of Obesity and Metabolic Surgery in a tertiary care referral center in India. Results were analyzed under three groups as follows.

Group A—patients who underwent bariatric surgery (BS) for PCOD (married and unmarried)
Group B—patients who underwent BS for primary infertility
Group C—patients who became pregnant after BS (included in groups A and B)

Exclusion Criteria

Patients with primary ovarian insufficiency, endometriosis, secondary infertility, strong family history of infertility, uterine fibroids, and endometrial tuberculosis were excluded from our study.

Definitions

Polycystic Ovarian Disease

Polycystic ovarian disease (PCOD) was defined as a group of symptoms (based on the Rotterdam criteria), which was due to elevated androgen (male hormones) in females [10–12].

Rotterdam Criteria

PCOD diagnosis should meet any two of these following criteria: (a) clinical hyperandrogenism (Ferriman–Gallwey score ≥ 8) or biochemical hyperandrogenism (elevated total/free testosterone); (b) oligomenorrhea (< 6–9 menses/year) or oligoovulation; (c) polycystic ovaries on ultrasound (≥ 12 antral follicles in one ovary or ovarian volume ≥ 10 cm^2) [13, 14].

Infertility

Infertility was a disease of the reproductive system, which was defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse [15].

Small for Gestational Age

Small for gestational age (SGA) was defined as a weight below ten percentile for gestational age [16, 17].

Terms of Pregnancy

Terms of pregnancy 37–38 weeks are defined as early pregnancy, 39–40 weeks a full-term pregnancy, 41 weeks a late pregnancy, and 42 weeks a post-term pregnancy [18].

Terms of Low Birth Weight

Low birth weight had been defined as first weight recorded within hours of the birth of ≤ 2500 g. Very low birth weight (VLBW) is accepted as < 1500 g, and extremely low birth weight (ELBW) as < 1000 gm [19].

Maternal Anemia

As per the global library of women's medicine, maternal anemia was defined as hemoglobin level < 11 gm/dl during pregnancy [20].

Statistical Analysis

Data were collected and analyzed. The responses to questions were reported as frequencies or percentages. Statistical analysis was done using SPSS version 20.0 (SPSS Inc., IL, USA). For continuous variables, results were shown as mean ± standard deviation (SD). For continuous variables, paired *t* test was used, while the chi-square test was done for categorical variables. Significance was considered when the *p* value was < 0.05.

Results

Seventy-one patients underwent BS in our study. Among them, 45 patients had completed 3 years of regular follow-up. Of the total of 45 patients who underwent bariatric surgical procedures, 40 patients underwent LSG, 4 patients RYGB, and 1 patient LAGB, respectively. Among the 45 patients, 16 married patients had a history of infertility who failed to conceive with assisted reproductive technique (ART) (group B). Twenty-nine patients had symptoms of PCOD (group A) who fulfilled the Rotterdam criteria.

Group A

Twenty-nine patients with PCOD symptoms were included in this group. Mean age of this group was 24.7 ± 10.2 years and mean BMI before surgery was 41.5 ± 6.8 kg/m^2. Among the 29 patients, 25, 3, and one patient underwent LSG, RYGB, and LAGB, respectively. They achieved 66.9% ± 24.0% excess weight loss and 76.6% excess BMI loss at the end of 3 years. Improvements in PCOD symptoms are presented in Table 2.

Group B

Sixteen patients with primary infertility were included in this group. The mean BMI before surgery was 48.5 ± 7.9 kg/m^2 and mean BMI during conception was significantly reduced to 31.8 ± 6.3 kg/m^2 ($p < 0.001$). Among 16 patients, 7 (43.75%) ($p = 0.61$) gave live birth after surgery. Out of 7 patients who became pregnant, 3 (42.9%) patients conceived naturally, and 4 (57.1%) patients conceived after ART. All the women conceived in 21.4 ± 2.3 months. The patients in this subgroup achieved 67.4% of excess weight loss (%EWL) and 71.8% of excess BMI loss (%EBMIL) during conception. Nine patients (56.2%) did not conceive after surgery.

Group C

The intent of this group is to analyze the maternal complication for the patients post-BS. Out of 45 patients studied, 19 patients conceived and gave live birth. Twelve (63.15%) patients had an early term (37–38 weeks), and 7 (36.82%) patients had a full-term (39–40 weeks) pregnancy. There were no incidences of post-term pregnancy noted. Nine (47.3%) low birth weight (≤ 2.5 kg) children were born out of 19 patients. Mean body weight of LBW infants was 2.13 ± 0.8 kg. There were no congenital anomalies seen in any of the infants who were with LBW. Fourteen (73.6%) patients had a normal delivery, 5 (26.3%) patients had a cesarean section, while 7 (36.8 %) patients had an incidence of maternal anemia. There was no incidence of gestational diabetes and hypertension (Table 1).

Table 1 Percentage of maternal incidence

	No. of incidence	% of incidence
Early term pregnancy	12	63.1
Full-term pregnancy	7	36.8
LBW	9	47.3
Normal vaginal delivery	14	73.6
Cesarean section	5	26.3
Inadequate milk secretion	6	31.5
Maternal anemia	7	36.8
Blood transfusion, iron infusion	2	28.5

LBW, low birth weight

Discussion

Female reproductive health is essential for the development of a healthy nation. The same is affected by medical, psychosocial, and economic factors [21]. These factors could be classified into two major categories—gynecological and obstetrical. Obesity negatively impacts female reproductive health in both manners [22]. Our study aimed to project the effectiveness of bariatric surgery in all aspects of female reproductive health, such as PCOD symptoms, infertility, fetal, and overall maternal health.

PCOD is one of the most common causes of female infertility [23]. The recent prevalence of PCOD in India is 11.9%, as quoted by Choudhary A et al. [24]. Females with PCOD are more prone to develop metabolic syndrome [25]. These patients are at higher risk for infertility [26]. Characteristics which are associated with PCOD are central obesity (CO), higher prevalence of insulin resistance and also higher incidence of metabolic disorders such as T2DM, SHT, and dyslipidemia [27, 28]. Increased visceral fat leading to insulin resistance in patients with PCOD that remains unclear could be a potential mechanism for the same [29]. A study by Sam S et al. shows 40–80% of women suffering from PCOD were obese [30]. The complex nature and pathophysiology of PCOD had been attributed to increased waist circumference, insulin resistance, hypothalamic-pituitary-ovarian axis hormonal imbalance, and the immature follicular generation that resulted in anovulatory cycles [31]. Increased visceral fat was associated with a higher level of inflammatory markers in PCOD [32]. Elevated levels of circulatory insulin reduce the synthesis of sex hormone–binding globulin (SHBG) resulting in increased free testosterone in circulation [33]. Ovaries are highly sensitive to Luteinizing hormone (LH) in PCOD patient that in turn could be a cause for hyperandrogenism [34]. Management of PCOD has been based on symptomology and

weight loss by diet, and lifestyle changes are the primary steps of PCOD treatment. Improvement in PCOD symptoms with as little as 5% of excess weight loss has been shown in a study by Badawy et al. [35]. In our study, patients achieved 66.9% EWL and 76.6% EBMI lost to follow-up of 1–3 years. We observed that most of PCOD symptoms improved significantly after BS, as shown in Table 2. Similar results were found in a meta-analysis by Skubleny et al. and also in a prospective study by Escobar et al. as follow ($p < 0.001$ and $p < 0.005$), respectively [36, 37].

Infertility is a significant concern for many, which is now increasing in the current era. Obesity negatively impacts female infertility. Indians have reported a fertility rate of 2.303 children per women [38]. Various ART methods are available for treating infertility, and only 50–60% of couples receiving ART's achieve pregnancy, as depicted in a study by Rich Edwards et al. [39]. Obesity in the reproductive age group ranged between 24.2 and 28.3% according to study by Khan R et al. [40]. Most infertile women are overweight and obese in the category. There are only 5% chances of giving live birth in obese females as showed by Rich Edwards et al. [39]. Grodstein et al. found that anovulatory infertility was higher in the overweight and obese patients [41]. Obesity is contributing to increased conversion of androgen to estrogens in adipose tissue, which causes decreased GnRH by negative feedback. Therefore, affected hypothalamic-pituitary-gonadal-axis causes an irregular menstrual cycle [42–45]. According to the NICE guidelines, there was an improvement in fertility rate when the bodyweight reduced by 10% [46]. Considering the above perspectives and the close relationship between obesity and fertility trends, BS could play a significant role in the improvement of women's reproductive health. A study published by Merhi zo et al. showed that there could be a partial or complete alteration of reproductive hormone profile post BS [47].

Table 2 Symptomatic improvement of PCOD

Parameters	Before surgery	After surgery	*P* value
Hirsutism	11	10	0.827
Amenorrhea	17	2	0.001
Menorrhagia	8	2	0.048
Dysmenorrhea	6	6	1.000
Oligomenorrhea	5	1	0.102
DUB	14	1	0.001
Acne	3	2	0.655
Hair fall	2	3	0.655
Dark patches on the skin	3	2	0.655
T2DM	1	1	1.000
Hypothyroid	7	6	0.782

T2DM, type 2 diabetes mellitus; *DUB*, dysfunctional uterine bleeding

In our study, we observed a fertility rate of 43.75% after BS. It was also observed that there was a significant reduction of mean BMI before and after BS, from 48.5 ± 7.9 kg/m^2 to 31.8 ± 6.3 kg/m^2 ($p < 0.001$). Concordant results were shown in the studies by Marceau et al. and Deitel et al. with fertility rates improving to 46.9% and 88.9%, respectively, after BS [48, 49]. With the above results, it becomes imperative to conclude that BS could provide a significant positive impact on the fertility rate in the obese subset of the population.

In post BS, we observed that there was a significant incidence of early term pregnancy of 63.2% ($p = 0.005$) while low birth weight was 47.4% ($p = 0.819$) (Table 3). Studies by Wax et al., Patel et al., and Richard et al. showed an incidence of SGA post-bariatric surgery as 26.3%, 26.9%, and 12.3%, respectively [50–52]. Equivalent results were found in studies by Wax et al. and Chevrot et al., where % of LBW post-bariatric surgery was 7.7% and 9–29% [50, 53]. It was observed that we had a higher incidence of SGA and LBW in our study when compared with these studies. The possible explanation to the above results could be related to the Indian cultural context where most people consume low protein and overall a poor nutritious intake pattern.

Developing nations like India bear a double-edged sword with undernutrition on one side and obesity on the other. The study by Laura et al. showed that maternal obesity significantly increased the risk of fetal macrosomia [54]. This study also showed that pre-pregnancy weight reduction could help to avert fetal macrosomia. Bariatric surgery could reduce the occurrence of fetal macrosomia, but at the same time, it also increases the possibilities of LBW simultaneously. Hence, there should be a necessity of bariatric-obstetric team approach while handling post-bariatric pregnancies and to obtain optimum outcomes.

It is well proven that maternal obesity has been strongly associated with maternal and fetal morbidity during the time of delivery [55, 56]. Obesity causes an increased risk of C-section, as shown in a study by Kaplan et al. [57]. It has been found out that leptin and cholesterol which are higher in obese patients causing poor uterine contractility due to less calcium ion (Ca2+) influx in the myometrium, which seems to be a pathophysiology factor for patients landing up in C-section in obese patients [58–60]. Prevalence of C-section in India was estimated to be around 17.2% between 2015 and 2016 [61, 62]. We have observed an increasing trend since then. In a

Table 3 Group C post-bariatric maternal outcomes

Total no.	Clinical conditions	Yes	%	*p* value
19	Pre-term delivery	12	63.2	0.005
	Low birth weight	9	47.4	0.819
	Normal vaginal delivery	14	73.7	0.019
	Maternal anemia	7	36.8	0.251

study by Berendzen JA et al., there was an increased prevalence of C-section in the obese population and which found to be 39–59% [63].

In our study, we found a statistical increased in rates of normal vaginal delivery rate of 73.7% ($p = 0.019$) when compared with a C-section rate of 26.3% post-bariatric surgery (Table 3). A study by Lapolla et al. showed a reduction of C-sections to 45.9% after bariatric surgery compared with 65.8% C-section in obese pregnancies which did not undergo any treatment for weight loss [64]. Our study finds coherence and also finds its support from studies done by Wax JR et al., Kjaer MM et al., and Josefsson A et al., where they found a significant reduction of C-section (18.3–60 %) following bariatric surgery when compared with patients who had undergone any treatment for obesity [50, 65, 66].

Anemia during the natal period is one of the most important factors associated with several maternal and fetal complications. In a study by Munasinghe et al., the authors quoted that the causes of maternal anemia could be due to deficiencies in the nutritional components like iron, folate, vitamin B_{12} and vitamin A [67]. Anemia has also been associated with increased risk of intrauterine growth restriction (IUGR), premature deliveries, LBW, maternal mortality, and stillbirths. Anemia is found to decrease the women's reserve to tolerate bleeding either during or after childbirth, hence increasing the propensity to develop infections in the natal and post-natal period. India has been found to have a prevalence of maternal anemia of 65–75% as shown in a study by Vanamala et al. and Kalaivani K et al. [68, 69]. We found that the incidence of maternal anemia in post-BS patients was 36.8% ($p = 0.251$) (Table 3). Optimization of anemia if diagnosed pre-operatively was done by iron and folic acid supplements. As per our institutional protocol and recommendations, we gave supplements of vitamin B_{12}, calcium, and multivitamins for a minimum period of 6 months post-surgery. During the subsequent follow-ups, if the patient developed anemia, iron and folic acid supplements were given after investigating the cause for the same. A study by Victoria et al. has also shown a higher risk of maternal anemia in mothers with a prior history of BS [70]. A significant ($p = 0.002$) rate of maternal anemia was seen in a study by Galazis N et al. [71]. We did not observe any adverse effects such as congenital malformation like fetal macrosomia in our patients' post-bariatric surgery. Post-bariatric surgery maternal anemia needs to be monitored properly, and iron replacement to be done at the earliest (Figure 1).

Postponing pregnancy for 1–2 years after bariatric surgery has been suggested [72,73]. This timeframe could be helpful to decrease hormonal instability in mothers, which may improve the necessary healthy nutritional environment to the fetal growth as emphasized in studies by Kominiarek MA et al., Leung TY et al., and Mansourian AR et al. [74–76]. Careful coordination with the bariatric surgeon and obstetrician is needed to avoid inadvertent complication to the mother and the baby.

Limitations

Our study was a single institutional, retrospective study. PCOD improvement was subjectively estimated by symptomatic relief; however, biochemical or ultrasound imaging was not used in the post-operative period. Gestational diabetes, inadequate lactation, maternal nutritional supplementation, nutritional deficiency, Apgar score in newborn, and post-delivery weight gain were not analyzed in our study. We also

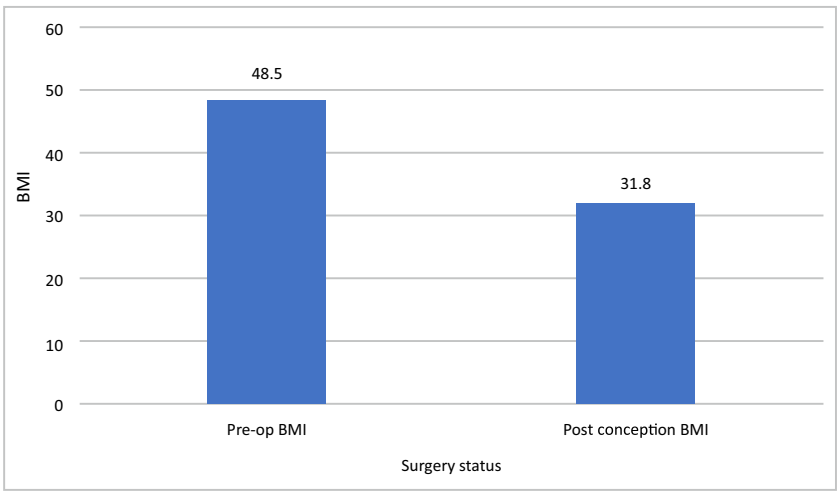

Fig. 1. Pre and Post conception BMI

could not study pre-operative psychological assessment and also post-bariatric quality of life (QOL) assessment.

Conclusion

BS could provide significant improvements in menstrual abnormalities, primary infertility, and also maternal outcomes in addition to substantial weight loss. Although ART techniques may be necessary for many, their results enhance significantly post-bariatric surgery. Reasonable care from the first trimester is essential to tackle the higher incidence of SGA birth, LBW, and maternal anemia post weight loss surgery. Adequate follow-ups could improve maternal and post-natal infant outcomes with proper coordination between obstetric and the bariatric team.

Compliance with Ethical Standards

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

Consent Consent had been attained from the patients before the surgery

Ethical Clearance The institutional ethical committee had approved the study.

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