

Fertility and perinatal issues in pregnancy after bariatric surgery

Abstract

Obesity is one of the most important public health problems today. In 2008, over 1.4 billion adults over 20 years old were overweight. Of these, 200 million men and 300 million women were obese. Bariatric surgery is an important and increasingly utilized treatment for morbid obesity and its complications. Approximately 40% of all bariatric patients are reproductive-aged women. Obesity during pregnancy is an important risk factor for bad pregnancy and perinatal outcome. According to the American College of Obstetricians and Gynecologists, in the United States more than one third of women are obese, more than half of the pregnant women are overweight or obese, and 8% of reproductive-aged women are morbidly obese. This review focuses on the effects of bariatric surgery on obese, reproductive-aged women that became pregnant after the surgical intervention. Although obesity is associated with subfertility regardless of the mode of conception (natural, ovulation induction, in vitro fertilization), fertility improves soon after bariatric surgery, especially in women who had been anovulatory.

Keywords: obesity, bariatric surgery, fertility, pregnancy

Obesity

The number of obese individuals nearly doubled since 1980. In 2008, over 1.4 billion adults over 20 years old were overweight. Of these, 200 million men and 300 million women were obese.

Overweight and obesity are defined by the World Health Organisation as the excess adipose tissue that can affect the health status of a person. Obesity is evaluated using the body mass index (BMI), the weight of a person in kilograms divided by square of the individual height in meters. The BMI correlates with the amount of adipose tissue, but it is not an exact representation of the excess fat. The amount of adipose tissue can also be evaluated by measuring the abdominal circumference, hip circumference or by ultrasound or magnetic resonance imaging. A person is obese when the calculated BMI is above 30 kg/m² and overweight when the BMI is over 25 kg/m²(¹).

Obese and overweight people are at risk in developing a large number of diseases, including: cardiovascular diseases (mainly heart disease and stroke), diabetes, musculoskeletal disorders (especially osteoarthritis - a highly disabling degenerative disease of the joints), some cancers (endometrial, breast, and colon)(¹).

Obesity during pregnancy is an important risk factor for bad pregnancy and perinatal outcome. According to the American College of Obstetricians and Gynecologists (ACOG), in the United States more than one third of women are obese, more than half of the pregnant women are overweight or obese, and 8% of the reproductive age women are morbidly obese. Every obese pregnant woman has a high-risk pregnancy regardless of the presence of gestational diabetes(^{1,2}).

The Prevalence of Obesity in Reproductive Age Women

The prevalence of obesity in reproductive age women in the United States according to National Health and Nutrition Examination Survey study in 2009-2010 is 31.9% in women aged between 20 and 39 years old. In the European countries the prevalence of obese women is variable: 36.5% in Poland (HAPIEE study) and 6.2% in France(³).

The Effects of Obesity on Fertility

Obesity is very common in women suffering from polycystic ovarian syndrome (PCOS). The major features of the PCOS include anovulation, menstrual dysfunction (caused by chronic anovulation) and hyperandrogenism, but may include obesity and metabolic syndrome, diabetes, hirsutism, infertility. In women with PCOS that lose weight and take Metformin, the ovulatory function tends to ameliorate, because one of the factors that generate ovulatory dysfunction is insulin resistance syndrome. Obese women with normal ovulatory function need more time to get pregnant and the pregnancy rate is lower than in normal weight women with normal ovulatory function. It is possible that certain factors related to obesity may affect the ovarian function, the oocytes and the ability of the endometrium to suffer the modification needed for nidation.

Certain studies suggest poorer outcomes of infertility treatment in obese women, insufficient follicular development, lower ovocyte count, while others report outcomes that are comparable to nonobese women, but higher doses of ovulation inducing agents need to be

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used. The risk of failed *in vitro* fertilization increases with increasing BMI and may be related to poor ovocyte quality, endometrial quality or other factors⁽⁴⁻⁹⁾.

Prenatal Issues

Obese pregnant women are exposed to a higher number of prenatal issues than the normal weight pregnant women. Obesity increases the risk of medically indicated preterm delivery due to obesity-related maternal disorders: hypertension, diabetes, preeclampsia, although obesity is not associated with an increased risk of spontaneous preterm birth.

Another prenatal issue that can occur, is hypertension. Maternal weight and BMI are independent risk factors for preeclampsia, and the risk of preeclampsia doubles with each 5-7 kg/ m² increase in prepregnancy BMI. Women with BMI over 30 kg/m² are at increased risk of miscarriage when compared with women with normal BMI. The excess risk of miscarriage in overweight and obese population is independent of embryonic aneuploidy and may be related to polycystic ovarian syndrome or isolated insulin resistance syndrome.

Obese pregnant women are at risk for developing gestational diabetes at a higher prevalence than the general obstetrical population: 6-12% vs. 2-4%. The prevalence of gestational diabetes increases by 0.92% for every increase of 1kg/ in BMI⁽¹⁰⁻¹³⁾.

Intrapartum Issues

The overall characteristics of labor progress are dependent upon maternal weight, so overweight and obese women have a longer first stage of labor than normal weight women (duration of labor from 4 to 10 cm was 7.5, 8 and 6.5 hours). By extending the first

stage of labor, obesity is in part responsible for a higher incidence of neonatal complications.

The rate of failed trial of labor after cesarean delivery is increased with maternal weight. In normal weight women is 15%, 30% in obese women and 39% in severely obese women. So, obesity increases the rate of cesarean delivery. Another important issue generated by the excess weight is macrosomia, a very common situation in babies of overweight and obese mothers, and it is an important risk factor for shoulder dystocia during labor^(14,15).

Postpartum Issues

The most important postpartum issues are postpartum hemorrhage, infection and venous thromboembolism. The increased frequency of postpartum hemorrhage in obese women is due to an increased frequency of macrosomia or reduced bioavailability of uterotonic agents at standard doses because of the relatively large volume of distribution. There is a high risk for postpartum infection in obese mothers regardless of the mode of delivery and despite the use of prophylactic antibiotic regimens. The prevalence of venous thromboembolism is higher in pregnancy and in obese individuals than in general population. The ACOG advice for use of pneumatic compression devices at the time of cesarean delivery⁽¹⁶⁾.

Bariatric Surgery

Bariatric surgical procedures are performed on obese or overweight patients in order to improve health by achieving long-term, durable weight loss. Restrictive operation restrict the amount of food intake by reducing the quantity of food that can be consumed at one

Table 1 Metabolic surgery in United States (March 2014)

	2011	2012	2013
Total number of interventions	158,000	173,000	179,000
Roux-en-Y gastric bypass	36.7%	37.5%	34.2%
Gastric banding	35.4%	20.2%	14%
Sleeve	17.8%	33%	42.1%
Biliopancreatic diversion or Duodenal switch	0.9%	1%	1%
Revisions	6%	6%	6%
Others	3.2%	2.3%	2.7%

time. Malabsorptive procedures limit the absorption of nutrients and calories from ingested food by bypassing the duodenum and a variable length of small intestine. The first bariatric procedure (the jejunocolic bypass - anastomosis between the proximal jejunum and ascending colon) induced weight loss by malabsorptive mechanism. Today, bariatric surgical procedures combine the malabsorptive mechanism with restriction, interfering with nutrient absorption, insulin resistance and alimentary behaviour (Table 1).

Bariatric surgery expanded rapidly in the last few years, over 340 000 surgical procedures being made in 2011 in the world. Over 150 000 bariatric surgery procedures are performed each year in the United States, and in Asia the number of bariatric surgical procedures grew by 449% between 2005 and 2009.

Roux-en-Y gastric bypass is the most common bariatric surgical procedure performed today. About 65% of the bariatric surgical procedures performed in 2003, were Roux-en-Y gastric bypass, and 45% in 2011. A vertically oriented proximal gastric pouch measuring 15-30 ml is created using a linear endoscopic stapler and then it is linked to a Roux jejunal limb of 75-150 cm in length. In this way, two intestinal limbs are obtained: the alimentary limb (the gastrojejunal anastomosis) and the bilio-pancreatic limb that contains digestive enzymes (gastric, biliary and pancreatic). The mechanism that leads to durable weight loss is restrictive (the small volume of the gastric pouch and the small diameter of the gastro-jejunal anastomosis) but also malabsorptive (the digestive enzymes are in contact with the food for a shorter period of time). Roux-en-Y gastric bypass has demonstrated not only to prevent the progression of non-insulin-dependent diabetes mellitus, but also to reduce the mortality from diabetes mellitus.

Durable control of diabetes mellitus is achieved following gastric bypass, along with amelioration or resolution of other comorbidities such as hypertension, sleep apnea and cardiopulmonary failure. Mean excess weight loss ranges from 69 to 82% with follow-up of 24 months.

Laparoscopic adjustable gastric banding - is a restrictive bariatric surgical procedure that involves the placement of an adjustable silicone band around the proximal stomach a few centimeters below the gastroesophageal junction. In this way, a small volume gastric pouch is obtained (just under 30 ml) that determines rapid onset of satiety after the ingestion of a small quantity of food. As an advantage, laparoscopic adjustable gastric banding is an easy to perform surgical procedure, completely reversible, with the lowest mortality rate of all the bariatric procedures (0-0.5%). The adjustable nature of the band allows the amount of restriction to be increased or decreased depending upon the patient's weight loss. Although it has many advantages, laparoscopic adjustable gastric banding is performed less frequently (24% of all the bariatric surgical procedures performed in 2003, and only 18%

of all the bariatric procedures performed in 2011), probably because of the frequent revisions and weight loss failure (weight gain caused by frequent intake of fluid, high energy content foods that can pass very easily through the narrowed stomach).

Vertical sleeve gastrectomy (gastric sleeve) is a restrictive bariatric procedure that was performed at the beginning as the first step of a more complex procedure called biliopancreatic diversion with duodenal switch. Later on, gastric sleeve became a stand-alone bariatric procedure because it is less expensive and has similar weight loss results, comparable impact on obesity comorbidities and fewer complications than other procedures.

Because gastric sleeve is technically easier to perform in a shorter surgical time, it became the second most frequent bariatric surgery procedure performed today in the world (28% of all the bariatric surgery procedures performed in 2011). The mechanism of weight loss in gastric sleeve procedure is mainly restrictive (the new stomach has a smaller volume and, because of the absence of the gastric fundus, a low capacity of distension) but also hormonal (by removing a large part of the stomach, including the gastric fundus, the number of ghrelin secreting cells is reduced). After undergoing gastric sleeve bariatric procedure, the patients have a lower insulin resistance, and higher serum levels of glucagon-like peptide-1 and YY peptide (intestinal hormones that reduce appetite and hunger sensation). Mean excess weight loss ranges from 50 to 60% with follow-up of 24 months.

Clinical Trial Studies

Many clinical trials have evaluated the biological modification that occur on women who underwent a bariatric surgical procedure.

Most oligomenorrheic women resumed normal menstrual cycles after 3 to 6 months postoperatively. The weight loss obtained after bariatric surgery, improves the metabolic and hormonal profiles in women suffering from PCOS - lower insulin resistance, lower androgenic levels.

A clinical trial⁽¹⁷⁾ evaluated pregnancy outcome in obese women that conceived following bariatric surgery. The results showed that 47% of the obese women that could not become pregnant before surgery, were able to conceive following bariatric surgery. The prevalence of fetal macrosomia reduced to 7.7% (the prevalence of fetal macrosomia in obese mothers is 34.8%) and 90% of the mothers reported a normal weight gain during pregnancy.

Another issue is to set the right time of conception after bariatric surgery. One observational study⁽¹⁸⁾ showed that the pregnancy outcome is not affected by the time to conception after surgery, but according to the ACOG, women are advised to delay pregnancy for 12 to 18 months following bariatric surgery in order to optimize weight loss and reduce the potentially adverse effect of post-bariatric surgical nutritional deficiencies.

Table 2

Perinatal outcomes after bariatric surgery: results of the nationwide population based matched cohort study

	Total	Small for gestational age	Large for gestational age
Births in women after bariatric surgery	2511	243 (5.2%)	188 (4.2%)
Births in obese women	12 379	750 (3%)	621 (7,3%)
Births in the general population	1 732 679	86 830 (2.3%)	74 906 (3.7%)

Contraception in reproductive aged women that underwent a bariatric surgical procedure is very important due to enhanced fertility associated with durable weight loss. Pregnancy rates in adolescents following bariatric surgery is two-fold higher than in the general adolescent population of the same age⁽¹⁹⁾.

Although this is probably due to enhanced fertility, gastric bypass procedure seems to reduce the absorption of oral contraceptives. This is the reason why the ACOG released a practice bulletin in June 2009 that recommends the use of non-oral forms of contraception in women who have undergone malabsorbtive bariatric surgery.

A recent nationwide population based cohort study made in Sweden⁽¹¹⁾ analyzed 1.7 million births that occurred between 1992 and 2009 in order to evaluate the prevalence of premature births, small for gestational age infants and large for gestational age infants. After analyzing the data, 2500 in births, the mothers underwent a bariatric surgical procedure before conceiving. The results showed that these mothers, had a greater risk of premature birth (9.7% vs. 6.1% in obese

women without surgery), and a greater probability of giving birth to a small for gestational age infant (5.2% vs. 3% in obese women without surgery), but a lower risk of giving birth to a large for gestational age infant (4.2% vs. 7.3% in obese women without surgery) (Table 2).

Conclusions

Although obesity is associated with subfertility regardless of the mode of conception (i.e. natural, ovulation induction, *in vitro* fertilization), fertility improves soon after bariatric surgery, especially in women who had been anovulatory.

Compared to women with BMI under 25 kg/m² (normal weight), pregnant obese women are at increased risk for pregnancy-related hypertension, gestational diabetes mellitus, and shoulder dystocia. After bariatric surgery, the risk of preeclampsia, gestational diabetes mellitus, and macrosomia decrease significantly, but the risk of intrauterine growth restriction or small for gestational age infant is higher than in the obese women population. ■

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