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Bariatric surgery and reproduction-implications for gynecology and obstetrics

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ABSTRACT

As the rates of obesity continue to rise across the world, there has been an increasing resort to bariatric surgery amongst the options for treatment. Through the reproductive lifespan, between menarche and menopause, women might benefit from this surgical intervention, which may have a bearing on other aspects of their health. The consequences of bariatric surgery have been reported and evaluated from various perspectives in obstetrics and

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Endocrine effects
Obstetric risks

gynecology. Fertility and sexuality are enhanced, but not all gynecological diseases are ameliorated. There are also psychological and behavioral sequelae to be cognizant of. With multidisciplinary and responsive care, most post-bariatric pregnancies have satisfactory outcomes. The effects of bariatric surgery on the babies conceived thereafter remains a subject of interest, whereas the possible effect on the climacteric is speculative.

Introduction

Obesity levels are increasing worldwide and have reportedly nearly tripled between 1975 and 2016. It is estimated that at least 2.8 million people die each year as a result of conditions that complicate being overweight or obese. The World Health Organization in 2016 estimated that there were about 1.9 billion overweight adults, of which 650 million had obesity (BMI $\geq$30 kg/m^2) (340 million adolescents and 39 million children); 39% (39% of men and 40% of women) were adults aged 18 years or over and were overweight, and 13% had obesity. The rise in obesity is not only in high-income countries, but also in low and middle-income countries [1]. Obesity is currently ranked among the top three social burdens consequent upon human behavior with an estimated annual cost of dealing with it and its complications at about USD 2 trillion, or 2.8% of the global gross domestic product (GDP) [2].

The relationship between obesity and women's health is well established. Women who have obesity are at a very high risk of various disorders/conditions, which affect almost all systems including the reproductive system. Fig. 1 shows some of the consequences of obesity.

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The spectrum of gynecological pathologies and conditions associated with or caused by obesity are shown in Table 1, whereas those associated with obstetrics are shown in Table 2.

Effective weight loss is central to minimizing the consequences of obesity (see Table 3). This can be achieved either non-surgically or through bariatric surgery. The surgery is often considered after ineffective non-surgical measures, which have been shown to be dependent on individual patient circumstances and motivation, societal perception of extremes of body build, and the acceptability of medical therapies towards weight loss. Bariatric surgery has been shown to treat Class III obesity, to indirectly reduce the burden of obesity-related morbidities, modify the course of metabolic disorders, such as diabetes mellitus and to ameliorate certain categories of hypertensive disorders. In this review, we discuss bariatric surgery and its role in managing morbid obesity. Furthermore, we examine the effects of bariatric surgery on reproductive health and the long-term implications of the procedure as related to reproduction.

Bariatric surgery

Bariatric surgery (BS) is increasingly being offered to those who have morbid obesity, the cases in which other non-surgical options of weight loss have failed.

The indications for bariatric surgery in general include failure of lifestyle modifications (which include integrating diet, exercise, behavioral modification, and psychological support), BMI >40 kg/m^2 or BMI> 35 kg/m^2 with serious coexisting co-morbidities, such as severe sleep apnea or life-threatening cardiopulmonary problems, diabetes, or joint disease [26]. Consideration may also be given to factors, such as psychological stability, high motivation, and the likelihood of surviving the procedure [27]. These indications vary from one country to another, being well regulated in some (e.g. the UK) and being offered on demand in others. Such an unregulated approach means some women would resort to surgery without attempting other options.

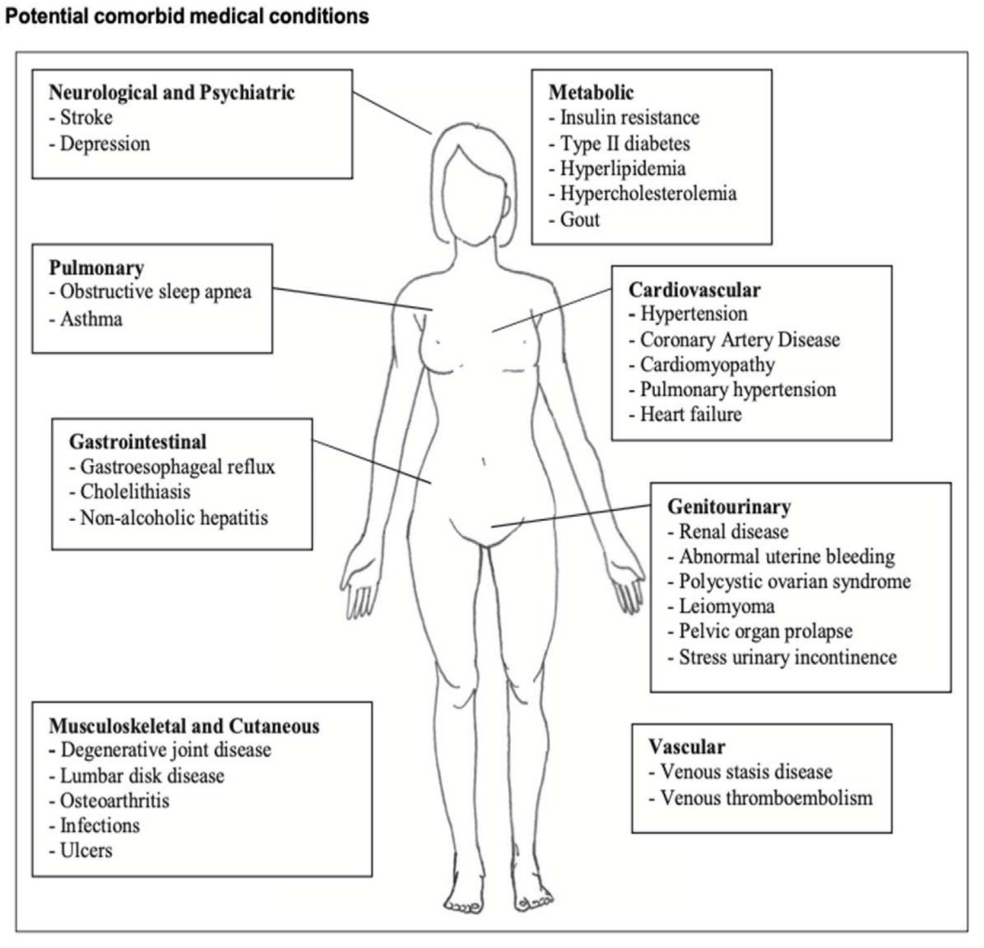

Fig. 1. Potential comorid medical conditions

The aim of bariatric surgery (BS) is to reduce caloric intake by modifying the anatomy of the gastrointestinal tract on the one hand and also by changing the absorptive bio-physiology on the other. Bariatric surgical procedures are classified as either restrictive or malabsorptive. The restrictive procedures limit intake by creating a small gastric reservoir with a narrow outlet to delay emptying while the malabsorptive procedures include introduction of bypasses in portions of the small intestine where nutrient absorption occurs. Examples also of restrictive procedures include gastric stapling (gastroplasty), adjustable gastric banding (wrapping a synthetic, inflatable band around the stomach to create a small pouch with a narrow outlet), or a combination of these two approaches and the vertical restrictive (sleeve) gastrectomy, in which much of the gastric body is resected leaving behind a narrow tube of stomach as an alimentary conduit by creating a small gastric pouch, which fills rapidly with early satiety [28]. Malabsorptive procedures include the Roux-en-Y gastric bypass (RYGB), biliopancreatic diversion (BPD), and duodenal switch. These procedures involve creating a bypass in a large section of the small intestines, thus reducing the surface area for absorption [28]. The proximal Roux-en-Y gastric bypass can be considered as a combined restrictive–malabsorptive procedure. It involves stapling of the stomach to create a small (≤30.0 ml) upper gastric pouch. The small intestine is

Table 1
Obesity-related conditions in Gynecology.

Polycystic Ovary syndrome [3]	Pre-disposition to Endometrial cancer [4]
Uterine fibroids [5]	Urinary incontinence [6]
Menstrual disorders - ranging from precocious puberty to abnormal uterine bleeding [7]	Depression and other psychiatric disorders related to unhappiness with body shape and size [8]
Progression in genital prolapse [9]	Adnexal lesions [10]
Sub-optimal oocyte quality in Assisted Reproduction Techniques [11]	Increase in minor complications, requiring higher doses of (Propofol) sedation and transabdominal retrieval during Assisted Reproduction Techniques [12]
Reduction of uterine receptivity in assisted conception cycles [13]	Sexual behavior and outcome differentials [14]

Table 2
Obstetric complications associated with obesity.

Spontaneous miscarriage [15]	Fetal death [16]
Pre-eclampsia [17]	Sub-optimal ultrasound imaging for fetal structural normality [18,19]
Gestational Diabetes [20]	Inadequate uterine activity in labor [21]
Postpartum hemorrhage [22]	Fetal Birth injury [23]
Congenital fetal malformations [24]	Labor dystocia and increased operative deliveries [25]

Table 3
Number of bariatric surgical procedures performed in the USA between 2011 and 2020 presented as figures every 3 years.

Type of BS	2011	2014	2017	2020
Sleeve	28,124	99,781	135,401	122,056
RYGB	57,986	51,724	40,574	41,280
Gastric Band	55,932	18,335	6318	2393
BPD-DS	1422	772	1588	3555
Revision	9480	22,195	32,238	22,022
Others	5056	193	5606	7397
Total	158,000	193,000	228,005	198,651

(The ASMBS total bariatric procedure numbers are based on the best estimation from available data (BOLD, ACS/MBSAQIP, National Inpatient Sample Data and outpatient estimations).

then divided at the mid-jejunum, and the distal portion (called the alimentary, or Roux, limb) is anastomosed to the gastric pouch. The distal portion of the stomach and proximal small intestine (the bilio-pancreatic limb) are anastomosed end to side farther down the jejunum. Food comes in contact with pancreatic and biliary secretions only below this anastomosis, in the segment of small intestine called the ‘common channel’. The shorter the common channel (and the longer the Roux limb), the less nutrient absorption will occur. Further details were earlier described by DeMaria [29].

Fig. 2 shows the various types of main bariatric surgical procedures. The most commonly performed procedure is sleeve gastrectomy. Figures published in 2019 show that of 520,983 BS were performed worldwide [30], 58.6% were sleeve gastrectomy, followed by gastric bypass (combined) (35.6%) and gastric banding (3.7%). Between 2020 and 2021, 311,441 bariatric surgical procedures were reported by 25 contributor registries from around the world. There was a female-to-male ratio dominance in 18 contributor registries, ranging from 9 to 1 in Azerbaijan to 5.8 to 4.2 in Kuwait. The pre-operative body mass index was 40–45 kg/m^2 in most cases, but was as low as 36.8 kg/m^2 in China. The median ages ranged between 25 years and 44 years. Sleeve Gastrectomy was performed in 61% of patients, followed by Roux-en-Y Gastric Bypass (26%) and One-anastomosis Gastric Bypass in 4.6%). These registries stated that there are more than 100 diseases that could potentially be improved by weight loss, and in the 2022 report, the most common pre-operative co-morbidity in those undergoing

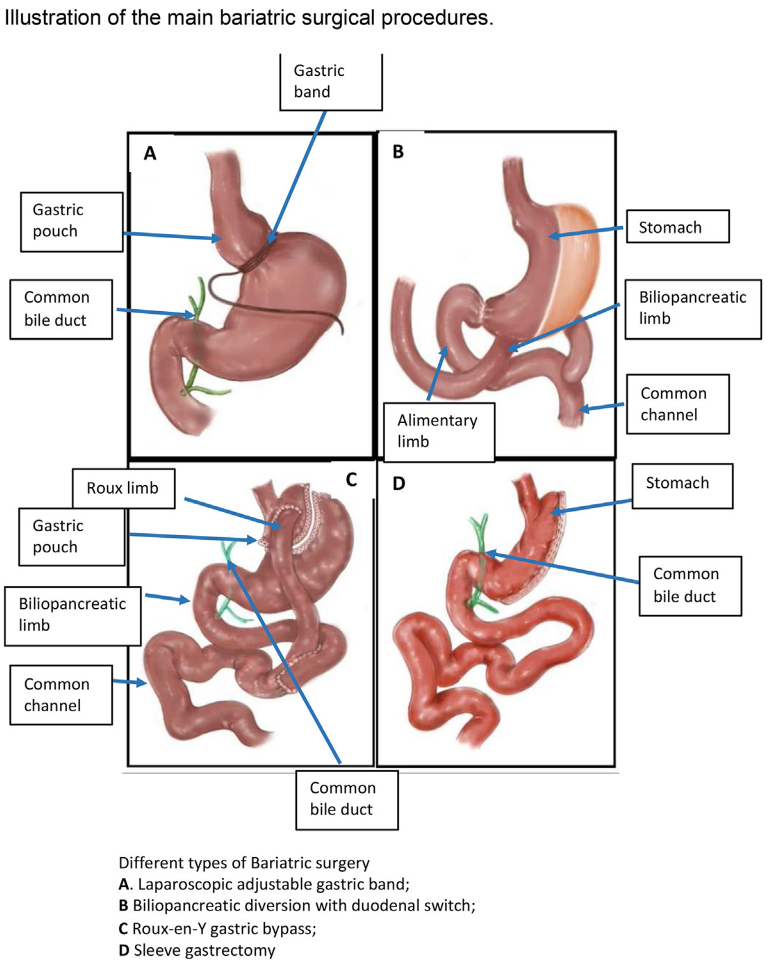

Fig. 2. Illustration of the main bariatric surgical procedures.

bariatric surgery was Type II Diabetes Mellitus [31]. Figures from the USA (Table 3) showed a steady rise to a peak around 2019 and thereafter there appears to be a fall. However, the data do not cover the period after 2020 [32].

Impact of bariatric surgery on weight

BS results in a faster and more sustained weight loss compared with behavioral and pharmacologic interventions [27]. In addition, the ensuing weight loss is associated with improvements in glucose homeostasis, dyslipidemia, hypertension, sleep apnea, gastroesophageal reflux disease, degenerative joint disease, urinary incontinence, quality of life, and even cancers [27,33,34]. The results of BS on weight are variable. Two large meta-analyses of this showed that patients with a pre-operative body mass index (BMI) of >40 kg/m^2 lose 20–40 kg over 2 years and maintained their reduced weight for up to 10 years [27,35]. For those who had gastric bypass and for whom the postoperative weight loss exceeded 45 kg (or approximately 65%–70% of the excess body weight and approximately 35%) of the BMI, the weight loss levelled off after 1–2 years, with patients regaining up to 10 kg after the weight loss nadir to a long-term plateau [27]. After laparoscopic adjustable gastric banding, the weight loss was approximately 50% of the excess body weight and approximately 25% of the BMI at 2 years [27]. Weight loss after vertical banded gastroplasty was approximately 50%–60% of excess body weight and approximately 25%–30% of BMI [27]. A plateau in weight loss was generally reached at 2 years after a slight weight increase from the weight response nadir [27]. This is an important time line as it is the period in which pregnancies are encouraged to be attempted after BS.

Complications of bariatric surgery include ventral hernia (up to 39%), gallstone disease (up to 20%), stricture (up to 15%), band slippage (up to 12%), pouch enlargement (up to 12%), small bowel obstruction (up to 10%), band erosion (up to 10%), ulceration (up to 9%), anastomotic leaks (up to 8%), severe esophageal dilatation (up to 3%), vomiting, diarrhea, bleeding, and vitamin deficiencies [27,36–39]. Rare but severe complications include fascial dehiscence (in up to 1%), pulmonary embolism and respiratory failure [39,40]. The mortality rate from bariatric surgical procedures is <1% [17,24,30]. Amongst the long-term complications are the dumping syndrome (5%–10%) resulting from influx of undigested carbohydrates into the jejunum, persistent vomiting, symptomatic cholelithiasis, and nutritional deficiencies [38–41]. Details of some of these complications are discussed in relation to the type of bariatric surgery.

Restrictive - adjustable gastric band complications

Complications of this procedure include mechanical problems with the band itself (e.g. band slippage and band, balloon, or tubing breakage), band erosion, acute obstruction, ischemia, and megaesophagus or pseudoachalasia. Re-operation for these complications is indicated in about 25% of cases [42].

Band slippage

Band slippage occurs when one wall or side of the stomach slips through the orifice of the band, resulting in a larger than normal gastric pouch superior to the band. It is considered the most common complication after laparoscopic adjustable gastric band [43,44] and occurs in 8% of patients [44]. It presents as a dilated gastric pouch superior to the band. These patients often report symptoms of immediate or delayed vomiting after meals, a feeling of fullness only relieved by vomiting, and occasional pain or irritation in the upper abdomen [45] (See Fig. 2).

Band erosion

In a small proportion of cases, band erosion was reported at rate of between 0.31% and 1.96% [46,47]. Patients frequently present with vague and non-specific symptoms of insidious onset. These include upper abdominal or back pain, loss of food restriction, melena stools, onset of reflux, or “spontaneous” infection of the subcutaneous band port (from bacteria from the gastric erosion tracking along the band tubing to the subcutaneous port) [45].

Megaesophagus or pseudoachalasia (enlarged esophagus)

Megaesophagus may be suggested by worsening dysphagia, regurgitation, or vomiting. Investigations reveal an esophagus dilated beyond the outer limit of the band. The dilation is thought to be due to chronic overeating, despite having a band to limit intake. As the esophagus expands and the capacity increases, patients describe loss of restriction (i.e. increasingly wanting to eat more) [45]. This complication does not require repeat surgical procedures treatment in most instances.

Gastric bypass procedures e.g. the roux-en-Y gastric bypass(RYGB)

This procedure results in a permanent alteration of anatomy.

Complications include gallstone disease, marginal ulceration, internal hernia, and intussusception [45].

Gallstone disease

Gallstone disease is more common following bariatric surgery when compared with the normal population [48]. Alterations in the enterohepatic circulation, hormonal changes associated with weight loss, and perhaps increased biliary stasis are believed to contribute to the development of cholelithiasis. The re-routing of food through the alimentary limb after RYGB may change or delay the release of the usual gut hormones that stimulate gallbladder contraction, resulting in atypical symptoms or non-postprandial abdominal pain.

Marginal ulceration

Ulceration of the anastomotic margins occurs in just under 5% of cases and usually follows the RYGB procedure [49]. Most occur at or near the gastro-junction anastomosis, but typical peptic ulcers in the first portion of the duodenum have also been described [50]. The most common symptoms are epigastric burning pain which occurs in approximately 57% of patients, followed by bleeding in 15% of patients [49].

Perforation

This may be spontaneous (1%–2% of patients) or those induced by factors, such as ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) or use of tobacco. Symptoms vary from mild (especially in those that occur spontaneously) to significant antecedent symptoms such as postprandial pain and nausea [29,51].

Bleeding

With the development of ulcers, bleeding may occur. This may be mild to moderate and occurs in about 5% of patients [52]. The symptoms are similar to those of any upper gastrointestinal bleeding and may include the passage of melena stools or hematochezia, hematemesis, and near-syncope or syncope if the bleeding is significant [51].

Small bowel obstruction

Small bowel obstruction may complicate RYGB procedures. This is related to internal hernias or postoperative adhesions. Occasionally this may be secondary to stenosis, or small bowel intussusception (often at the jejuno-jejunostomy site). The symptoms include diffuse abdominal pain, distension, bloating, nausea, and vomiting. It is important to recognize that bowel obstruction related to adhesions is more common after open procedures than laparoscopic procedures. Over 50% of small bowel obstructions are caused by internal hernias [53].

Internal hernia

A potentially catastrophic late complication of RYGB is the development of internal hernias. It may be very difficult to diagnose and is often associated with small bowel volvulus. Symptoms may be non-specific and intermittent. The overall incidence of internal hernias after RYGB is 2.5%, with most (87%) of hernias occurring at the transverse mesocolic defect [51].

Nutritional deficiencies

The nutritional deficiencies that occur after bariatric surgery depend to a large extent on the type of surgery performed [39,54]. These are least likely after restrictive procedures since none of the intestinal segments where absorption of these occur, is bypassed [39]. Malabsorptive procedures on the other hand are more likely to be complicated by serious nutritional deficiencies, especially when there is no supplementation after surgery [39]. The deficiencies are commonly those of vitamins B12, D, thiamine, and folic acid and the elements calcium, iron, zinc, and magnesium [39,54].

Endocrine consequences of bariatric surgery

Obesity affects reproductive physiology through changes in the hypothalamic-pituitary-ovarian (HPO) axis. These include altered pulsatile gonadotropin secretion (55,56,57,58), decreased urinary luteinizing Hormone (LH), follicle stimulating hormone (FSH), estradiol ($E_{2)}$ metabolite, and luteal progesterone (P) metabolite excretion as reported by Santoro et al. [55] in a large cohort of ovulatory women aged 43–55 years. Jain et al. [56] investigated the HPO axis in premenopausal women with morbid obesity and in normal-weight women and showed that in the former, the amplitude but not the frequency of LH pulses was preferentially dampened. It is thought that this alteration in the HPO axis is a factor in the reproductive dysfunctions that are common, especially in women with morbid obesity and is associated with changes such as decreased androgen levels [57], which cause a decrease in sex hormone binding globulins (SHBG) and a reduction in LH secretion thought to be secondary to impaired secretion of GnRH [58].

Post-bariatric weight loss has been shown to lead to a reversion of the altered reproductive hormone profile associated with morbid obesity [59–61]. Bastounis et al. [59] measured serum sex steroid levels in 38 premenopausal women immediately before and 12 months after vertical banded gastroplasty and found a decrease in E_2 and total and free testosterone and an increase in FSH and SHBG levels following the surgery. In their cohort, postoperative normalization of menstrual irregularities was reported in five women with concomitant weight loss. In another study, Victor et al. [61] found increased SHBG levels after bypass surgery in seven women with morbid obesity when compared with 14 controls. Amongst 40 women with morbid obesity, Gerrits et al. [60] showed a rise in SHBG, FSH, and LH levels with a concomitant decline in testosterone and DHEAS levels after biliopancreatic diversion.

Another hormone that has been investigated in women who have undergone bariatric surgery is the brain-derived neurotrophic factor (BDNF), a protein belonging to the neurotrophin family. BDNF is expressed in the ovaries, and is present in follicular fluid of women with normal menstrual cycles, the pre-ovulatory follicle of women undergoing IVF and in plasma [62–65]. This factor is thought to mediate LH and human chorionic gonadotropin (hCG) action in promoting preovulatory oocyte meiotic maturation [66]. BDNF was measured in the plasma of 18 women with morbid obesity before and 3 months after BS surgical weight loss [67] and levels were found to have fallen significantly in all the women suggesting that surgical weight loss, which results in reduced energy balance is likely to be responsible for this fall. This fall is associated with a favorable impact on LH and hCG levels [68].

In addition to the changes in the HPO axis associated with surgical weight loss, other changes in the hypothalamic–pituitary–adrenal (HPA) axis have also been reported. In a study of fertile women with morbid obesity, 2 years after biliopancreatic diversion, Manco et al. [69] found that cortisol-binding globulin(CBG) decreased, free cortisol index (FCI) (cortisol/cortisol-binding globulin) increased, and insulin secretion decreased, whereas insulin sensitivity increased significantly. BMI and body weight positively correlated to serum CBG, C-reactive protein, and leptin. Furthermore, increase in free cortisol was associated with a simultaneous decrease in CBG levels. It would seem from this study that the HPA axis adapts to a changing environment, leading to decreased CBG levels, a concomitant increase in the metabolically active free cortisol fraction, and an overall increase in FCI.

Type III obesity is associated with increased levels of Thyroid Stimulating Hormone (TSH) and subclinical hypothyroidism and is regarded as the most common endocrinopathy associated with it [70]. An additional benefit of BS in women with Type III obesity and subclinical hypothyroidism is therefore an improvement in thyroid function profile. In those who are overtly hypothyroid, weight loss may be associated with a dose reduction in thyroxine requirements [71]. Chikunguwo et al. [72] investigated thyroid function by measuring TSH and free Thyroxine (T4) in 86 women with Type III obesity and no previous diagnosis of thyroid disorder (10% of these had subclinical hypothyroidism) before and 6 months and 12 months after restrictive BS and found a significant reduction in TSH levels after the surgical weight loss. The change in BMI (drop) correlated positively with the drop in TSH. Interestingly, levels of free T_4 were not influenced by weight loss. Subclinical hypothyroidism resolved in all the cases after bariatric surgery. In another study of 72 women with Type III obesity (25% of whom had subclinical hypothyroidism) who had undergone the RYGB procedure, Moulin de Moraes et al. [73] measured TSH and free T_4 before and 12 months after the surgery and reported a significant post-surgical decrease in subclinical hypothyroidism (decrease in TSH but not in free T4).

In a systematic review, Azran et al. [74] showed that subclinical hypothyroidism was resolved in 87% of patients following bariatric surgery. In those with overt hypothyroidism, they found that, there was a statistically significant (95% CI: 19.69-6.71] reduction in the dose of levothyroxine. They also demonstrated that discontinuing or decreasing levothyroxine dose was significant following Roux-en-Y gastric bypass, anastomosis gastric bypass, and sleeve gastrectomy, (OR = 31.02, 95% CI [10.34, 93.08]), (OR = 41.73, 95% CI [2.04, 854.69]), (OR = 104.03, 95% CI [35.79, 302.38]), respectively.

A few studies have examined the outcomes of pregnancies in women treated for thyroid disease post-bariatric surgery. Treatment for subclinical hypothyroidism and hypothyroxinemia between the 8th and 20th week of pregnancy did not result in significantly improved cognitive outcomes in the resulting offspring, followed up until 5 years, compared to mother-baby pairs who were not exposed to treatment [75]. It is recommended that women with a BMI of 40 kg/m^2 and above should undergo thyroid function screening before or during pregnancy [76]. However, in post-bariatric pregnancies, in which the BMI of the patient has fallen below this but there is no personal or family history of diabetes or thyroid disease, clinical discretionary screening is implied.

Bariatric surgery and ovarian reserve

One possible effect of bariatric surgery on ovarian reserve was suggested by a study of women in their late reproductive age (ages 40–52 years). Su et al. [77] showed that the mean antral follicle count and ovarian volumes did not differ between women with obesity and normal-weight women. Mullerian-inhibiting substance (MIS) levels were, however, significantly lower (by 77%) in women with obesity than those in normal-weight women. Furthermore, Inhibin B levels were also lower (by 24%) in women with obesity compared with normal-weight women, although the difference did not reach statistical significance. Freeman et al. [78], in a study of healthy late reproductive-age women (ages 35–47 years) similarly reported an indirect relationship between obesity and MIS levels; they were 65% lower in women with obesity compared with normal-BMI women. When adjusted for menopausal status, age, race, and day of the menstrual cycle, BMI remained significantly associated with MIS levels. Taken together, these findings suggest that obesity negatively impacts ovarian function/reserve. Since these studies were conducted by including women who were nearing the end of their reproductive years, it is important to note that the results may not be applicable to much young women with obesity. It is speculated that follicular dysfunction, which is associated with morbid obesity may be a possible explanation, although the precise mechanism of this relationship is unclear [79,80].

Merhi et al. [67] investigated the relationship between BMI and ovarian reserve in 16 women before and approximately 3 months after bariatric surgery and found that MIS levels significantly dropped after surgical weight loss only in women aged less than 35 years. The drop was absent in perimenopausal women. MIS levels would be expected to rise after weight loss, but this was not the case in this study. It was speculated that malabsorption of critical precursors that may affect MIS gene expression, an effect of the surgery and/or the stress (with this as a transient finding) could be the explanation. In another recent study [Casals, Ventosa and Flores et al.], in women aged 19–40 years with a mean BMI of 43.9 kg/m^2 measured anti-mullerian Hormone (AMH), FSH, LH, estradiol, testosterone, SHBG, androstenedione 2, metabolic parameters (adiponectin, leptin, ghrelin, insulin) as well as antral follicle count with 2/3D ultrasound and showed that AMH levels fall significantly after BS and while AFC fall, this was not statistically significant. In a recent systematic review of eight studies [81], it was concluded that most of currently available studies report a decrease in AMH levels occurring 6 months and/or 12 months after surgery, suggesting ovarian reserve impairment following BS.

Fertility after bariatric surgery

Amongst the compounding factors that have a bearing on fertility outcome in women with obesity are chronic anovulation and disruption of the hypothalamic-pituitary-ovarian axis and the secretion of BDNF (see section on endocrine effects of BS). Although obesity does not universally affect fertility (as there are indeed regularly ovulating women with obesity who achieve successful pregnancies), it has been shown to be associated with high IVF cycle cancellation rates and low number of mature oocytes [82–84]. Other studies have shown that women with obesity have impaired response to ovarian stimulation and often require high doses to achieve satisfactory follicular growth [55], they have a lower chance of a live birth after IVF and intracytoplasmic sperm injection (ICSI) [82]. Even when pregnancies occur, these women are at a high risk of spontaneous miscarriage [85]. Although there are studies that conclude that obesity has no negative impact on ovarian stimulation in IVF cycles and no adverse impact on implantation in donor oocyte recipients, (i.e. obesity does not exert a negative effect on endometrial receptivity) [86], NICE and other national and international societies on the balance, recommend delaying offering assisted reproductive treatment to women with a BMI of >35 kg/m^2 (NICE, ESHRE), primarily because nonsurgical weight loss in women with morbid obesity improves fertility outcomes [87–89].

Weight loss following BS has been shown to improve menstrual cycle regularity and hormone profiles immediately after the surgery in women with Type III obesity [90]. Legro et al. [91] reported a sudden increase in sex hormone binding globulin, a reduction in androgens and an increase in follicle stimulating hormone (FSH) after bariatric surgery. Several studies have investigated hormonal changes following bariatric surgery and some reported a significant decrease in testosterone levels and an increase in SHBG after surgery [91–93], whereas others reported significant increases in estradiol [91,92] and SHBG, most peaking within one month after surgery [91] and lasting until 12 months [90,91]. Still in some, levels of FSH and luteinizing hormone (LH) did not change after the surgery [94]. A few studies reported that hirsutism resolved in women following bariatric surgery and suggested that this was most likely due to improved hormonal balance (especially the fall in androgens and the rise in SHBG) after the surgery [94,95].

In their systematic review, Moxthe et al. [94] reported significant improvements in menstrual cycle regularity and length in six out of eight studies. Menstrual cycles became regular at 12 months after RYGB in 85% of women with oligo-/amenorrhea, whereas the rate of irregular menstruation decreased from 60% to 20% after laparoscopic sleeve gastrectomy (LSG) [96], and menstrual dysfunction rate decreased by 12.4% after various bariatric surgical procedures [97]. Legro et al. [91] measured multiple menstrual cycle parameters in 9 patients and found mixed results. Obesity was associated with increased cycle length (due mainly to lengthening of the follicular phase -the mean follicular phase length was 6.5 days shorter within 3 months after surgery and 7.9–8.9 days shorter 6–24 months after; $p < 0.001$). An overall significant decrease in menstrual cycle length was observed at 6 months after surgery ($p = 0.04$) but not at 12 months. The shortening of the follicular phase in women with obesity was also reported by Grieger and Norman [98] - the mean follicular phase length was 6.5 days shorter within 3 months after surgery and 7.9–8.9 days shorter 6–24 months after surgery ($p < 0.001$).

Weight loss (nonsurgical) in morbidly obese women is well recognized to improve fertility outcome [85–87]. The data following bariatric surgery are variable with pregnancy rates varying from 30% to 100% [99]. Although the precise mechanisms for improved reproductive outcomes after bariatric surgery are not well understood, these may be related to several factors including regularity of menstrual cycles, changes in hormones towards a favorable endocrine milieu, improved quality of oocytes, increased ovulation, and increased sexual activity [100]. Most of the published studies failed to distinguish between ovulatory and anovulatory women with obesity [101,102].

In an interesting study on 24 amenorrheic women with polycystic ovary syndrome (PCOS), 5 women who lost about 57% of their weight after bariatric surgery conceived spontaneously [103]. Although the others did not conceive, they all resumed normal menstrual cycles by three months. Several other studies have reported improved conception rates that vary even in those who lost minimal weight to those who lost significant weight after BS [101,102]. Improvements in fertility outcome after bariatric surgery are not universal. Sheiner et al. [104], for example, reported a higher use of infertility treatments in patients who previously underwent bariatric surgery compared with the controls. While such studies are few, this would suggest that obesity is only one factor (rather than the only factor in question) in those presenting with infertility or subfertility. It is possible that in those in whom bariatric surgery fails to improve fertility outcomes, the metabolic changes following weight loss (e.g. those related to malabsorption of essential nutrients) may be contributors to the subfertility

[67]. This must be taken into consideration when counseling women undergoing bariatric surgery in the hope of improving fertility outcome.

Effects of bariatric surgery on fertility in men

Weight loss after bariatric surgeries in men has been shown to result in an increase in total and free testosterone levels, a reduction in estradiol levels as well as consistent improvements in sex hormones and sex hormone binding globulin (increase in both free and total testosterone and a fall in SHBG) [105–110]. In a meta-analysis of fertility after bariatric surgery, Moxthe et al. [94] combined three studies that compared hormones levels in men who had undergone bariatric surgery to a control of "no surgery" [107,108,111] and found significantly greater hormonal improvements in the bariatric surgery groups compared to the control groups.

With regard to semen quality, two studies examined semen or sperm quality and found these to have improved - one reported significant improvements in volume and sperm viability [107]. In contrast, the other reported that sperm count was significantly improved in a sub-group analysis indicating that patients with azoospermia or oligospermia had significantly increased sperm counts whereas those with normal sperm counts at baseline did not show any difference after the surgery [105]. Sperm volume, motility, or morphology did not show any difference in the sub-group analysis. Two other studies failed to report any significant improvement in seminal outcomes after bariatric surgery [106,111].

Pregnancy after bariatric surgery

Jamal et al. [95] reported a conception rate of 100% for previously infertile PCOS subjects with obesity who had undergone bariatric surgery. Four other studies reported improved pregnancy rates after bariatric surgery; seven out of 15 women who were unsuccessful in becoming pregnant became pregnant (46.7%) after laparoscopic sleeve gastrectomy (LSG) [96], five out of nine conceived after surgery (93), 83.3% of women who were unable to become pregnant were pregnant after intragastric balloon placement [112], and 62.7% who could not conceive, became pregnant after various surgeries [37]. Musella et al., in 2012 [113] also found that BMI and the degree of weight loss after surgery were significant predictors of pregnancy. In contrast, Goldman et al. [98] and Laurino et al. [114] reported no significant improvement in conception or pregnancy after bariatric surgery.

Miscarriage

Obesity is an independent risk factor for spontaneous first-trimester miscarriage [115,116] possibly through an unfavorable intrauterine milieu caused by sub-optimal endometrial receptivity and an altered hormonal environment of the developing oocyte [86,117]. This increased risk is in both spontaneously conceived and ART conceived pregnancies [115,116]. In a meta-analysis of 16 studies, Metwally et al. [118] concluded that obesity increased the risk of miscarriage irrespective of the method of conception. Few studies have, however, failed to demonstrate a negative effect of obesity effect on miscarriage risk [86,119]. Advocating for weight loss has been premised on the fact that this reduces the risk of miscarriage. Indeed, studies in women who lost weight without surgery showed a positive effect on miscarriage. Merhi et al. [120], Friedman et al. [121] and Bilenka et al. [122] investigated the effect of bariatric surgery on the risk of miscarriage. Again, these observations have not been universal - a study by Marceau et al. [123] found that the miscarriage rates before and after bariatric surgery were not significantly different. A 2021 systematic review and meta-analysis of 20 studies concluded that there was no difference in rates of miscarriage following bariatric surgery compared to those prior to the surgery [124]. It would therefore seem from these data that BS does not affect the spontaneous miscarriage rate. More data would be required to firm up this conclusion.

Nausea and vomiting

Excessive nausea and vomiting in early pregnancy with or without abdominal pain may be a source of concern in the post-bariatric patient, especially if such a pregnancy occurred in the first few months after the intervention. Surgical complications such as anastomotic leak, bowel obstruction, internal bowel herniation and gastric ulceration may occur. Up to 1.5% of pregnant post-bariatric patients might need a laparotomy or laparoscopy to address these and related complications [125].

Postprandial (dumping) syndrome may also complicate post-bariatric pregnancies. Only case reports appear to have been published on this. Dizziness, generalized flushing and feeling unwell, associated with palpitations are the typical features which tend to occur within an hour of a carbohydrate meal. There have been a few reports of symptoms such as hand tremors, occurring up to 2–3 h postprandially, and presenting in the second (but not the first) trimester [126]. Others have reported jitteriness and recurrence of symptoms a few hours after sub-optimal treatment, and a nocturnal pattern to the symptoms of hypoglycemia [127].

Post-gestational weight retention

Post-gestational weight retention may be an issue in women who have undergone bariatric surgery. If the index pregnancy occurred not too soon after the intervention, the observed weight retention may simply coincide with the trajectory of weight regain in non-pregnant post-bariatric women. Two recent studies have reported on this. A prospective study of 127 post-bariatric pregnant women was undertaken to investigate gestational weight gain, postpartum weight retention, and fetal growth. About 59% of the women gained more weight than is recommended by the Institute of Medicine guidelines and 24% had sub-optimal weight gain through pregnancy. Late preterm delivery (23%) and babies who were small for gestational age (47%) occurred in 23% of mothers who had insufficient weight gain. Mothers who gained weight in pregnancy were found to have retained an average of 7.1 kg (CI 5.5–8.7) by the 6th postpartum week. Between 16% and 21% of this cohort smoked, and the women's weight category at conception was scored as overweight or obese in 37% and 41%, respectively [128]. In a different study, which compared similar patterns between pregnant women who had undergone surgery, and those who had not, the proportions of gestational weight changes were comparable. Babies who were small for gestational age were no more likely to be born to mothers who had insufficient weight gain in the post-bariatric group. Overall, post-bariatric women had more babies that were small for gestational age and fewer large for gestational age babies [129].

Bariatric surgery and oral contraception

The efficacy of oral contraceptives depends partly on absorption from the gastrointestinal tract. Women with a BMI >40 kg/m^2 are generally not advised to take the combined oral contraceptive pill but may take the progestogen only contraceptive pill. This is because of some, albeit limited evidence, of a higher failure rate in women with morbid obesity [130] and an increased risk of venous thromboembolism [131]. Following bariatric surgery (especially the bypass type), gastrointestinal disturbances may affect absorption of contraceptive pills and therefore contribute to increased risk for unintended pregnancy [60]. In a study by Victor et al. [61] on seven women with morbid obesity (mean weight 129 kg preoperatively) aged 20–44 years, who underwent jejunoileal bypass (mean weight loss of 39 kg), plasma levels of hormones were lower after the ingestion of 3 mg norethisterone and 0.25 mg levonorgestrel in patients during the first 8 h after ingestion of the pills, compared with the levels in a control group of five non-obese healthy fertile women with a mean weight of 57 kg. The most probable explanation for the lower levels of hormones after bariatric surgery in this study may be that absorption was affected by the operation. It has also been suggested that the absorption of ethinylestradiol (a component of the combined oral contraceptive pill) may be reduced in bypass procedures that lead to decreased efficacy [132]. Reliability of the COC may also be affected by complications of BS, such as vomiting and diarrhea. With respect to progestogen only pills, evidence from pharmacokinetic studies has shown increased contraceptive failure in those who underwent jejunoileal bypass (a procedure which is less commonly performed today). The consensus from available evidence reviewed so far is that women who have undergone BS should avoid combined oral contraception and should instead use long-acting reversible contraception e.g. intrauterine devices and subdermal implants [133].

Bariatric surgery and sexuality

Obesity has been shown to be associated with a high risk of sexual dysfunction [90]. Furthermore, women with complications secondary to obesity have an increased prevalence of sexual dysfunction when compared with matched controls [134]. Hyperandrogenemia, insulin resistance, altered metabolic milieu, dyslipidemia and its related prescribed medications, as well as psychological problems associated with obesity have been suggested as possible mechanisms or contributing factors [135].

Obesity has also been shown to have an adverse effect on sexual desire and frequency of orgasm [136].

If obesity affects sexual function, would weight loss be beneficial? Kim et al. [137] reported a significant improvement in arousal, lubrication, orgasm, and sexual satisfaction in women (aged 28–44 years) after non-surgical weight loss using Sibutramine and behavioral therapy. In the study, those who achieved significant weight loss had a high degree of symptom improvement. Weight loss following BS has also been shown to improve sexual function [138]. In a study of 82 female patients with obesity who had undergone BS, Kinzl et al. [139] reported that 63% of the women had an increase in sexual satisfaction and interestingly 12% reported a decrease in sexual function after weight loss; 17% of these women had undergone surgery mainly to improve their sexual relations with their partner. Several other studies have reported similar improvements [140]. This effect was still demonstrated 1 year after bariatric surgery [141].

Two studies that examined sexual function, satisfaction, or intimate relationship reported mixed results. One study found a significant improvement in sexual function using the Female Sexual Function Index scale at 12-month follow-up [30], whereas the other study did not find any significant results in intimate relationship, frequency of sex, or sexual satisfaction [38]. Hammoud et al. (144) reported a positive association between bariatric surgery and male patients' sexual quality of life. The study by Legro et al. [106] did not show any significant improvement in male erectile function, but did show a trend of improvement by 12 months after surgery ($p = 0.13$). Reis et al. [111] used the International Index of Erectile Function (IIEF-5) questionnaire and reported a significant mean score improvement at 24 months after the surgery within the surgery group as well as a significant mean difference compared to the control group ($p < 0.05$).

Resolution of gynecological disease after bariatric surgery

In a recent meta-analysis of 21 studies including 552 women with polycystic ovary syndrome, Tian et al. [142] found that top-rank clinical and endocrinological features improved after bariatric surgery. However, the FSH/LH ratio did not change in the 3 months following surgery, although the levels of LH decreased.

Revisional plastic surgery and abdominoplasty

Following significant weight loss, most patients observe sagging or redundant skin in different body parts that may often require corrective esthetic surgery. The spectrum of post-bariatric contouring surgery encompasses abdominoplasty, chiplasty, cruroplasty, mastpexy, and panniculectomy with or without liposuction. Among these esthetic surgeries, abdominoplasty is reported to have the highest complication rate. The complications include seroma and hematoma formation, wound dehiscence, fat and skin necrosis, and wound scarring on the long term [143].

One important surgical issue of concern apart from body contour esthetic interventions, relate to displacement of the umbilicus (a useful landmark for laparoscopic surgery), unsuspected hernias and risks of wound infection and breakdown. The importance of abdominal examination especially for loss of sensation is underlined by a systematic review of abdominoplasty-related nerve injuries [144]. Pooled data from 25 publications showed that the lateral femoral cutaneous nerve was directly injured in 1.36% of patients, whereas the iliohypogastric nerve was injured in 0.10% of patients. Decreased sensation over the ipsilateral abdominal wall was 7-fold as common as chronic pain.

Alsulainy et al. [145] reported the presence of abdominal adhesions at laparoscopy for acute abdominal pain long after bariatric surgery. Awareness of, and resort to alternate laparoscopy access sites would seem prudent in the management of post-bariatric abdominal pain and in these cases, bowel herniation must be considered as a possible cause [146,147].

Emotional changes after bariatric surgery

Published reports indicate the need for thorough pre-operative psychological evaluation and risk assessment. From a systematic review and analysis of 32 studies of which more than 75% were on women, Castaneda et al. [148] found that attempted self-harm risks were higher in women who had undergone bariatric surgery (OR 1.9; CI 1.25−2.95) compared to age and BMI-matched controls (OR 3.8; CI 2.19−6.59). It was suggested that pre-surgical emotional eating or depressive illness might have been a risk factor, as these are more common in those with high BMI. Other behavioral problems that have been reported include alcohol abuse [149] and persistent opioid use [53,150].

Obesity-related gynecological cancers

When malignancy is diagnosed in the reproductive years, therapeutic interventions may significantly interrupt or effectively end a woman's childbearing potential. Sexuality may be adversely affected, and acceptable or safe contraception options may be limited. Resort may then be made to embryo freezing, surrogacy and child adoption. Emerging clinical studies indicate that, within the first 5 years following bariatric surgery, there is a lowering of the overall risk of breast and endometrial cancer, as well as Non-Hodgkin lymphoma [151]. This benefit on breast cancer risk appears to be mainly related to the menopausal years, and especially in those who have a combination of abnormal glucose metabolism and excessive adipose tissue (acting as precursor sources of endogenous estrogens).

Other possible benefits of bariatric surgery for obesity have emerged from the analysis of the US National Inpatient Sample data between 2010 and 2014 [152]. Subjects who had a family history of malignancy and a BMI above 35 kg/m^2 who had not undergone bariatric surgery subsequently had a two-and-a-half times higher rate of breast cancer compared to those with the same predisposition in the case cohort (18% vs 7.5%, $p = 0.0991$). Because the mean age of both control and study group was above 50 years, it is unlikely that this finding is applicable to women of reproductive age. Some important observations in patients after bariatric surgery were the possible increased risk of colorectal cancer, Barrett metaplasia, and esophageal cancer [153]. Long-term follow-up and surveillance are therefore essential.

Downstream benefits on offspring

It is desirable that the benefits, which follow bariatric surgery in women of reproductive age not only improve their own subsequent obstetric, gynecological and post-reproductive outlook, but also that such benefits are conferred on their subsequent offspring. Two important studies from two continents, examined this and found diametrically opposite findings. In 2006, Kral et al. [154] undertook a retrospective study of 172 children born to mothers with obesity in Canada, before and after bilio-pancreatic bypass surgery. Follow-up data were available in nearly 90% of the offspring of 45 mothers before surgery and of 172 mothers after surgery, for durations ranging between 2 years and 18 years. The pre-operative mean BMI in 35 mothers was 57.1 ± 8.5 kg/m^2 and subsequently dropped by 15 units or more. There was no indication of the mother's age or parity at the time of index conception following maternal bariatric surgery, the prevalence of obesity in the offspring decreased by 7%.

A record-linkage study of women who had given birth before and after bariatric surgery was analyzed from the Swedish Medical Register of Births between 1980 and 2008 [155]. In the 71 child-mother-child triads in which complete relevant information was available, there were no demonstrable differences in the sibling's BMIs at the 4th year of life. None of the mothers were hypertensive or diabetic. Most of them (72%) had undergone either vertical banded gastroplasty or gastric banding. The regression model had been adjusted for maternal age, education, and birth order.

To explore related changes at a sub-molecular level, 25 offspring born to 20 unrelated mothers before and after they underwent a duodenal switch procedure for severe obesity were studied in Quebec, Canada by Guenard et al. [160]. There was a 90% follow-up rate. Gene analysis from blood samples from the subjects, taken between the 2nd year of life and the 25th year, showed that 5698 of probes were differentially methylated, correlating with functionally-relevant gene expression. The enabling effect of the intervention is plausible. Whether this benefit follows both malabsorptive or restrictive techniques of bariatric surgery remains to be seen.

The interest in this aspect of post-bariatric surgery underlines it is perceived relevance in patient counseling and in the design of long-term surveillance of resulting offspring.

Conclusion

The Obstetrician and Gynecologist may be the influential healthcare professional who nudges the woman with morbid obesity towards bariatric Surgery, given the reality of her existing or pre-existing clinical profile. Reassurances need to be given about the safety of the procedure, its superior effectiveness over non-surgical options for weight loss and long-term overall health benefits. The reproductive health consequences may be short or long-term, but are not uniform and as such, Clinicians need to keep abreast with evolving long-term surveillance data and debates, regionally and globally, for patient counseling and information.

Practice points

- A patient with morbid obesity may be encountered for the first time in the obstetric and gynecology service, or after she has undergone bariatric surgery. The clinician needs to be aware of the spectrum of associated diseases and systemic dysfunctions.
- The main consequences of bariatric surgery in the reproductive age female are alterations in menstrual cyclicity, improvement of hormonal milieu, enhancement of endocrine-related subfertility and a possible need for esthetic surgery for the consequent redundant skin and subcutaneous tissue.
- Pregnancy management involves recognition of acute gastrointestinal accidents which may require laparoscopy or laparotomy, use of alternate strategies in screening for diabetes, and correction of vitamin and mineral deficiencies.
- Co-incidental or emerging mental health issues should not be missed, particularly if there has been a resort to substance or alcohol overuse. So too, is also the potential alteration in risk of certain malignancies.

Research agenda

- Impact of new pharmaco-therapeutic agents for weight management on women with morbid obesity in the reproductive age including followed up on possible/unexpected effect(s) on both the women and offspring long-term health.
- Well-designed multi-center cohort and interventional studies in post-bariatric pregnancies focusing on the best interval between bariatric surgery and pregnancy, interventions after surgery to improve pregnancy outcomes bariatric surgery related complications in pregnancy.
- Consideration of establishing a repository for data on pregnancies after bariatric surgery locally, nationally, and internationally for comparisons and generation of data.
- Prospective studies on the endocrine changes following bariatric surgery including new, less invasive options, or those options that are tailored particularly to women's needs.

Q1. From the IFSO Report of 2022, the most common co-morbidity that was associated with bariatric surgery was:

A. Infertility.
B. Obstructive Sleep apnea.
C. Type 2 Diabetes Mellitus.
D. Morbid obesity.
E. None of the above.

Answer: A = F; B = T; C= F; D = F; E = F.

Explanation. The 7th International Federation for the Surgery of Obesity and Metabolic Disorders Global Registry Report revealed that Obstructive sleep apnea was the most frequent co-morbidity in patients who underwent bariatric surgery in the study period. It was more likely in male patients and was noticeable in China, South Africa, Canada, and France. The other co-morbidities reported were Diabetes, Hypertension, Dyslipidemia, and Gastroesophageal Reflux Disease. A female preponderance was noted for Depression.

Q2. Post-bariatric weight loss reaches a nadir at:

A. 3 months.
B. 6 months.
C. 9 months.
D. 12 months.
E. 24 months.

Answer: A = F; B= F; C= F; D = T; E = F.

Explanation.

The maximum weight loss following bariatric surgery is between 12 and 18 months.

Q3. The possible esthetic, endocrine, and metabolic consequences of bariatric surgery include all of these except:

A. Need for dose adjustment in pre-existing LevoThyroxine therapy.
B. Adrenal disorder.
C. Increase in serum Anti-Mullerian hormone.
D. Vit B12 deficiency.
E. Need for an Abdominoplasty.

Answer: A = F; B= F; C = T; D = F; E = F.

Explanation.

Outside and in the course of pregnancies that follow bariatric surgery, a need to reduce the overall dose of replacement LevoThyroxine has been reported in keeping with a normalization' or reduction of serum Thyroid Stimulating Hormone.

Adrenal insufficiency is a rare consequence of bariatric surgery, which may manifest at variable times thereafter. Features are fatigue, nausea, and weight loss.

Decreased levels of Anti-Mullerian hormone are reported after bariatric surgery.

Because bariatric surgery affects mostly the absorptive function of Vitamins B1, B2, B3 and B9 subsequent deficiencies are to be expected. Although Vit B12 levels are already inadequate in some pre-bariatric surgery patients, deficiency is usually demonstrable within months following surgery in most patients.

Although the first recorded dermolipectomy' was performed in 1890, it has undergone progressive modification and improvement since then. It has become the most popular choice of procedure following bariatric surgery. Other important options for achieving post-bariatric tissue tone and skin surface area reduction range from liposuction to suction-assisted lipectomy to high intensity focused electromagnetic technology to attain an acceptable body contour. It was the most often performed procedure after massive weight loss procedures, others being mastopexy, upper arm lift, lower body lift, and thigh lift in 2020 as reported by the US National Clearing House of Plastic Surgery Procedural Statistics.

Q4. Regarding post-bariatric pregnancy, one or more of the following statements are correct:

A. In contravention to advice of the Metabolic Team, a significant proportion of women do get pregnant within 24 months.
B. If a woman who quite recently underwent Roux-n-Y bariatric surgery presents with severe abdominal pain and vomiting a Surgical consult is more time-critical, than a Physician consult.
C. Preterm delivery rates are not higher than in the background obstetric population.
D. Oral Glucose Tolerance Tests are not validated for Diabetes screening.
E. Post-pregnancy weight retention is rare.

Answer: A = T; B = T; C = T; D = T; E = F.

Explanation.

They do. Either deliberately or inadvertently.

Persistent nausea and vomiting in pregnancy are not to be dismissed, as these may be the presenting features of mechanical complications of bariatric surgery.

Patient intolerance and inaccurate results are the important limitations of subjecting a post-bariatric pregnant woman to the oral Glucose Tolerance Test. A surgical consult is best sought early, supplemented by the appropriate imaging method.

It has been shown that adherence to the recommended ranges of weight gain in pregnancy is not always achievable. Consequently, postpartum retention of weight is significant and more likely to persist especially if there is a short interval before another pregnancy is embarked upon.

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