Comorbidities of obesity and preconception counselling

Consideration of bariatric surgery

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THE PREVALENCE OF OBESITY in Australian women of reproductive age is increasing alarmingly. In the decade between 2008 and 2018, the prevalence of obesity in women aged 25–34 years rose by 110%, and in women aged 35–44 years by 56%.[1,2] Comorbidities of obesity, including type 2 diabetes (T2D), chronic hypertension and obstructive sleep apnoea (OSA), are associated with an array of significant fetal, neonatal and maternal risks during pregnancy (Table 1). Maternal obesity alone is associated with increased risk of infertility, miscarriage and adverse pregnancy outcomes (Table 1). In 2017, 21% of Australian women were obese at their first antenatal visit.[3] The first-line treatment of obesity is the role of general practitioners (GPs) in providing lifestyle, behavioural and motivational approaches to achieve sustained weight loss. The efficacy of lifestyle measures in resolving comorbidities of obesity and improving fertility may be limited in magnitude and sustainability. The National Institute for Health and Care Excellence guidelines recommend considering bariatric surgery for individuals with a BMI >40 kg/m^2 or those with BMI >35 kg/m^2 in the presence of other comorbidities where other weight loss measures have proven unsuccessful.[4]

The aim of this article is to examine the risks and benefits of bariatric surgery prior to pregnancy in women with morbid obesity, particularly where complicated by comorbidities of excessive weight.

Effect of lifestyle measures and bariatric surgery on pregnancy outcomes

GPs have a crucial role in providing preconception counselling for women who are obese. Lifestyle interventions may be limited by women being desirous of conceiving in the near future, difficulty in maintaining motivation with regard to lifestyle changes, frustration with slow gains achieved and lack of awareness of the maternal and fetal risks of maternal obesity in pregnancy. A recent Cochrane review examined the benefits of preconception lifestyle advice on weight versus routine care in women who were obese.[5] Studies were identified only in women with obesity and infertility. The evidence was very low quality; however, no benefits were seen with lifestyle advice with respect to number of live births, gestational diabetes mellitus, hypertension or miscarriage. Another study of primary maternal lifestyle interventions attributed limited success to late implementation, poor adherence and/or generic guidelines.[6] Analysis of a longitudinal cohort of Australian women found that obesity was negatively associated with aspirations for pregnancy in the next 5–10 years; however, no lifestyle or psychological factors were associated with intentions for having children in this time period.[7] An integrative review of preconception care to reduce the risks of obesity in women of reproductive age noted limited attention and interest by healthcare professionals, which may contribute to women's unawareness of these risks to preconception health.[8] GPs have a primary role in identifying, educating and counselling reproductive-aged women with obesity on the relationship between maternal obesity and infertility and adverse pregnancy outcomes, and where the woman is receptive to change, in initiating lifestyle measures.

The potential benefits and risks of bariatric surgery with respect to maternal, fetal and neonatal outcomes in future pregnancies need to be carefully considered on an individual basis. A systematic review and meta-analysis of the maternal and neonatal outcomes in pregnancy in women who were obese found that previous bariatric surgery was associated with reductions in gestational diabetes mellitus (odds ratio [OR]: 0.2), large-for-gestation-age (LGA) infants (OR: 0.31), all hypertensive disorders of pregnancy (OR: 0.38), postpartum haemorrhage (OR: 0.32) and caesarean delivery (OR: 0.5) when

compared with pregnancies in control women with obesity.[9] However, pregnancy after bariatric surgery was associated with increased risk of small-for-gestational-age (SGA) infants (OR: 2.16), fetal growth restriction (FGR; OR: 2.16) and preterm delivery (OR: 1.35). There was no difference in rates of malformations, stillbirth, neonatal death and neonatal intensive care admissions following bariatric surgery. When compared with laparoscopic sleeve gastrectomy (LSG), gastric bypass surgery (GBS) is associated with an increased risk of SGA infants, maternal anaemia, nutrient deficiencies, dumping syndrome and surgical complications during pregnancy, although a lower risk of LGA infants.[10] Other obstetric and medical outcomes are comparable between bariatric surgery types.[10]

Preconception maternal weight loss following bariatric surgery is associated with a reduction in obesity and adverse cardiometabolic profile in their babies, which persists into adolescence.[11]

Effects of lifestyle measures and bariatric surgery on comorbidities of obesity and fertility

Several studies have compared the outcomes of bariatric surgery with lifestyle intervention regarding remission of comorbidities of obesity.

Intensive lifestyle interventions in non-pregnant adults with obesity over a duration of 3–6.5 years resulted in complete remission of T2D and hypertension in 0–14.8% and 12.4% of participants, respectively.[12,13] A one-year intensive lifestyle intervention resulted in remission of OSA in 40% of individuals who were morbidly obese.[14]

Bariatric surgery has been shown to result in complete remission of T2D in 47–78%, remission of hypertension in 31–75% and remission/improvement of OSA in 79–86% of individuals who are obese.[14–16]

Assessment of the effect of bariatric surgery on PCOS is complicated by significant heterogeneity and small numbers in published studies. GBS was associated with resolution of menstrual abnormalities in 82–100% and remission of T2D in 77.8% of women.[17] LSG resulted in restoration of normal menstrual pattern in all 132 women with PCOS and menstrual irregularities, and four of 11 patients unsuccessfully treated for infertility preoperatively became pregnant postoperatively. Twenty-two per cent of women with PCOS and obesity became pregnant within 12 months post LSG.[18]

Bariatric surgery has been shown to be associated with longer life expectancy than usual obesity care.[19]

Bariatric surgery may have benefits in improving fertility in women who are obese with respect to both natural pregnancy and assisted reproductive technology (ART), whereas lifestyle interventions have not been shown to be of significant benefit. A systematic review and meta-analysis of the impact of preconception lifestyle interventions in subfertile/infertile women who were obese found an increased natural pregnancy rate but no difference in live

Table 1. Relative risk of adverse pregnancy outcomes with obesity and related comorbidities

	BMI 30–34.9 kg/m²	BMI >35 kg/m²	T2D	OSA	Chronic hypertension	PCOS
Miscarriage	1.3[42]	2.5[42]	1.3[43]	1.0[44]	1.0-2.3[45]	3.0[46]
Congenital malformations	1.2–1.9[47]	1.5[47]	1.7–6.0[43]	1.3[44]	1.4–2.0[48]	1.2–1.4[49]
GDM	2.7[50]	4.1–4.6[50]	–	1.9[51]	1.6[52]	2.8–3.4[53]
Gestational hypertension	2.1[50]	2.6[50]	–	–	–	4.1[53]
Pre-eclampsia	1.43[50]	3.0[50]	1.9-2.5[43]	2.3[54]	7.7[55]	3.3–4.2[53]
Pre-term birth	1.2[50]	1.2–1.7[50]	2.8-4.2[43]	2.3[56]	2.7[52]	1.3–2.2[53]
Macrosomia	2.1[57]	2.6–3.1[58]	4.7[43]	–	2.0[52]	1.0–1.6[59]
Perinatal mortality	1.7[50]	2.0–3.1[58]	2.5-8.9[43]	2.0[60]	2.0-4.0[52]	1.5–3.1[61]
LSCS	1.3–1.6[57,62]	1.8–2.0[62]	1.7[43]	2.0[44]	2.7[52]	1.7[59]
SGA	–	0.6–0.9[50]	0.7[43]	2.7[54]	2.7[52]	1.2–4.6[59]
Thromboembolism	2.7–14.9[63]	–	1.0[43]	4.5[64]	1.6[52]	–
Maternal mortality	2.2[65]	3.4[65]	–	5.3[64]	4.8[66]	–

–, no data available; BMI, body mass index; GDM, gestational diabetes mellitus; LSCS, lower segment caesarean section; OSA, obstructive sleep apnoea; PCOS, polycystic ovary syndrome; SGA, small for gestational age; T2D, type 2 diabetes

birth rate, birthweight or pregnancy complications.[20] A cohort study of women who were morbidly obese found that prior bariatric surgery was associated with significantly higher chances for pregnancy (adjusted hazard ratio [aHR]: 2.89), successful delivery (aHR: 2.78) and vaginal delivery (aHR: 6.42), and lower peripartum complications than control women.[21]

In 2010 it was estimated that 4.1% of women who gave birth in Australasia received some form of ART. Lifestyle intervention prior to in vitro fertilisation did not improve embryo utilisation rate or cumulative live birth rate in women with obesity.[22] In women with obesity and infertility seeking ART, prior bariatric surgery was associated with a reduction in the length of stimulation required, a higher number of fertilised oocytes and an increase in pregnancy and live birth rate.[23] The age at which bariatric surgery is performed to improve fertility may be important. Bariatric surgery in women >37 years of age is less likely to be beneficial, as the negative effects of increasing age on fertility are likely to outweigh the benefits of bariatric surgery for improved fertility with weight reduction.[24]

Risks of bariatric surgery

Immediate and long-term adverse effects, both general and those specifically related to pregnancy, must be discussed in detail when considering bariatric surgery. Major surgical complications following LSG in the general population include gastric leaks (2%), haemorrhage (1.1%), splenic injury (0.1%), later stenosis (0.9%), postoperative gastroesophageal reflux (6.5%), abscess (0.7%) and death (0.2%).[25] The rate of revision following LSG was 4.7% at five years. Major surgical complications in series of laparoscopic GBS were anastomotic leak (2%), bowel obstruction (2.9%), haemorrhage (1.9%), wound infection (3%), stomal stenosis (4.7%), ventral hernia (0.4%) and death (0.2%).[26] Following laparoscopic GBS, 8.1% of individuals required revision surgery.[27]

Considerable evidence shows short- and medium-term improvement in depressive symptoms following bariatric surgery, and suicide rates following bariatric surgery (0.3%) are lower than in the general population (1.4%).[28] However, a subgroup of patients exhibits erosion of these improvements or new onset of depression. Some studies have found an increased risk for suicide among patients post bariatric surgery.[29] GPs have a pivotal role in monitoring for deterioration in mood and psychological adjustment following bariatric surgery.

Micronutrient and vitamin deficiency following bariatric surgery are significant given increased risks of SGA, FGR and premature delivery. An Australian study of non-pregnant adults who were overweight/obese found the prevalence of micronutrient deficiency to be significant for vitamin E (31%), vitamin A (100%), vitamin D (89%), folate (72%), iron (5.5%) and zinc (99%).[30] Deficiencies of zinc, thiamine, folate, copper, vitamin A, vitamin B1 and vitamin B12 were found in in less than 10% of non-pregnant individuals in the USA at multiple time points within two years following bariatric surgery.[31] Serum vitamin D was <75 nmol/L in 37%, and serum ferritin <30 ng/mL in 25% of individuals.[31] A French study testing for nutrition in each trimester of 57 singleton pregnancies in women with previous bariatric surgery found deficiencies of vitamin A in 21–40%, vitamin D in 8–33%, vitamin C in 41–83%, thiamine in 15–45%, folic acid in 0–14% and selenium in 22–78%.[32] It is recommended that ferritin, 25OH-vitamin D, calcium, phosphate, folate, active vitamin B12, prothrombin time, magnesium and zinc be checked preconception and in each trimester, and additionally that vitamin A, thiamine and selenium be measured in the first trimester.[33] Vitamin A replacement should be limited to 10,000 IU/day, as higher doses in the first trimester are teratogenic.[34] GPs have a key role in monitoring for nutrient deficiencies in the long term in all patients post bariatric surgery.

A systematic review examining the impact of bariatric surgery on breastfeeding found that breastmilk after bariatric surgery is adequate in nutrients, energy and vitamin A, and no adverse effects were reported in breastfed infants when maternal nutrient deficiencies were corrected.[35,36]

Symptomatic late dumping/reactive hypoglycaemia in non-pregnant individuals is uncommon, having been reported in only 0.1–1.2% of individuals following bariatric surgery. Dumping syndromes are far less common following LSG than GBS.[37]

Surgical complications including internal hernia, small bowel obstruction and cholelithiasis represent the greatest risk for pregnant women following bariatric surgery. A systematic review of 120 cases of women with previous bariatric surgery requiring emergency surgery during pregnancy reported that 99 women (82.5%) had undergone previous GBS, 17 women (14.2%) had undergone previous laparoscopic adjustable gastric banding, and one woman had undergone previous LSG.[38] Maternal death occurred in three (2.5%) cases, while fetal death occurred in nine cases (7.5%). Authors have estimated a rate of diagnostic laparoscopy or laparotomy of 1.5% in the first pregnancy after bariatric surgery, compared with 0.1% in a control group of pregnant woman with obesity.[39] A high degree of suspicion for surgical complications is required by health professionals because of the non-specific nature of symptoms, which may be otherwise attributed to normal pregnancy. Prompt diagnosis should be pursued with rapid surgical exploration where clinical or radiological signs are suggestive of pathology.

Timing of pregnancy after bariatric surgery

Recommendations for women to avoid pregnancy for 12–24 months after bariatric surgery to enable stabilisation of maternal weight are based on consensus recommendations rather than clinical evidence. Two recent retrospective cohort studies compared pregnancy outcomes between women who fell pregnant within 12 months of bariatric surgery and those who deferred pregnancy until later than 12 months after bariatric surgery.[40,41] In the two cohorts, 36.8% and 22.1%

of women, respectively, conceived within 12 months of bariatric surgery despite advice that pregnancy should be delayed. The authors found that maternal weight gain was greater and vitamin B12 deficiency less prevalent in the group that conceived after 12 months; however, there were no differences in hypertensive disorders, gestational diabetes mellitus, mode of delivery, gestation of delivery, preterm delivery, birthweight, SGA infants or FGR between the two groups.

Sleeve gastrectomy or bypass procedure?

No studies have specifically addressed the most appropriate bariatric surgical procedure for women of reproductive age.[33] LSG may be preferable to GBS as the latter is associated with significantly greater risk of surgical complications during pregnancy, late dumping syndromes, maternal anaemia, nutritional deficiencies and FGR.[10] Future studies comparing the benefits and risks of restrictive versus malabsorptive bariatric surgery in women of reproductive age desirous of future pregnancy who are morbidly obese would be useful to guide health professionals regarding the optimal procedure for this group. GPs' awareness of the relative risks of the different surgical techniques for future pregnancy is important in counselling reproductive-aged women considering bariatric surgery.

Conclusion

The prevalence of obesity in reproductive age women in Australia is increasing rapidly. Maternal obesity and its comorbidities are associated with a significantly increased risk of adverse maternal and fetal outcomes, as well as reduced fertility. First-line management of obesity is provision of lifestyle, behavioural and motivational approaches by GPs to achieve sustained weight loss. Studies examining the potential benefits of more prolonged preconception lifestyle interventions in women with obesity would be valuable. Where lifestyle measures are unsuccessful, and particularly where significant maternal comorbidities of obesity are present, consideration of careful and sensitive discussion of the benefits and risks of bariatric surgery may be worthwhile with interested women.

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Competing interests: None.

Funding: None.

Provenance and peer review: Not commissioned, externally peer reviewed.

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