**Review Obesity: impact on obstetric practice and outcome**

Authors Frances M Stewart / Jane E Ramsay / Ian A Greer

**Key content:**
- Prepregnancy obesity is increasingly common.
- More than half of all women who died from direct or indirect causes in the 2003–05 report, *Saving Mothers’ Lives*, were overweight or obese.
- Obese mothers have an increased risk of complications.

**Learning objectives:**
- To learn about the increased incidence of miscarriage, congenital malformation and metabolic complications.
- To learn about the increased risks of intrapartum complications.

**Ethical issues:**
- Should medical assistance to conceive be withheld until BMI ≤35?
- More of the healthcare budget should be spent on prevention rather than treatment of obesity.

**Keywords** congenital abnormality / deep vein thrombosis / gestational diabetes mellitus / hypertension / perinatal mortality


**Author details**

**Frances M Stewart MD MRCOG**
Consultant, Obstetrics and Gynaecology
Antrim Area Hospital, Bush Road, Antrim, County Antrim BT41 2RL, UK
Email: francesstewart1@hotmail.com (corresponding author)

**Jane E Ramsay MD MRCOG**
Consultant in Obstetrics and Gynaecology
Ayrshire Maternity Unit, Crosshouse Hospital, Kilmarnock KA2 OBE, UK

**Ian A Greer MD MRCP(UK) FRCP FRCPI FFFP FMedSci FRCOG**
Consultant in Obstetrics and Gynaecology
Hull York Medical School, University of York, Heslington, York YO10 5DD, UK

© 2009 Royal College of Obstetricians and Gynaecologists
Introduction

The 2003–05 report of the Confidential Enquiries into Maternal Deaths in the United Kingdom highlighted obesity as a significant risk for maternal death. More than half of all women who died from direct or indirect causes were either overweight or obese.

For the mother, obesity increases the risk of obstetric complications during the antenatal, intrapartum and postnatal period, as well as contributing to technical difficulties with fetal assessment (Box 1). The offspring of obese mothers also have a higher rate of perinatal morbidity and an increased risk of long-term health problems.

The epidemiology of obesity

The prevalence of obesity, defined as a body mass index (BMI) ≥ 30 kg/m², has significantly increased during the last three decades, both in the USA and other countries in the developed world. American trends are now seen among the European population. In a health survey of England, the Department of Health reported that 32% of women aged 35–64 years are overweight (BMI 25–30) and 21% are obese (BMI >30). In a British Women’s Heart and Health Study, one-quarter of the 4000 participants in England, Scotland and Wales were found to be clinically obese. One-fifth of the women were inactive and two-fifths did not eat one portion of fresh fruit a day. The Department of Health has predicted that, if current trends continue, by 2010, 6 million women in England will be obese. In line with this, a large Scottish maternity hospital has observed a two-fold increase in the proportion of women with a booking BMI >30 over the last decade. Obesity amongst women is of worldwide concern, as shown in Australia by Callaway et al. in 2006. They noted that 35% of Australian women aged 25–35 years were overweight or obese. Obesity accounts for >280 000 deaths annually in the USA and will, if current trends continue, soon overtake smoking as the primary preventable cause of death.

Antenatal health issues

Obesity is associated with an increased risk of first trimester and recurrent miscarriage and fetal anomaly, in both women with polycystic ovary syndrome and those with normal ovarian morphology. A meta-analysis of 13 studies looking at gonadotrophin-induced ovulation in women with normogonadotropic anovulatory infertility found obesity and insulin resistance to be the most clinically useful predicting factors for poor clinical outcome. The incidence of spontaneous miscarriage has been reported to rise as insulin resistance increases. It has been suggested that insulin-sensitising agents, such as metformin, also reduce miscarriage rates. One potential mechanism for this observation is an increased production of inflammatory and prothrombotic agents produced by adipose tissue or released from endothelium secondary to stimulation by adipocyte-derived factors. It has been suggested that plasminogen activator inhibitor-type 1 (PAI-1) is associated with increased rates of miscarriage in association with maternal obesity. Treatment with metformin appears to reduce PAI-1 and miscarriage rates.

Several studies have shown up to a two-fold increase in risk for neural tube defects where there is pre-pregnancy maternal obesity. The greater the maternal BMI, the higher the risk of congenital malformation. It is well recognised that maternal diabetes is a risk factor for the development of congenital abnormality, including central nervous system defects. A cumulative effect on the risk of central nervous system birth defects when maternal obesity and gestational diabetes coexist has also been highlighted. Anderson et al. evaluated an American population in a case control study (n = 477). After adjusting for maternal ethnicity, age, education, smoking, alcohol use and periconceptional vitamin use, obese women still had substantially increased risks of delivering offspring with anencephaly (odds ratio [OR] 2.3, 95% CI 1.2–4.3), spina bifida (OR 2.8, 95% CI 1.7–4.5) and isolated hydrocephaly (OR 2.7, 95% CI 1.5–5.0). When gestational diabetes was examined in isolation, the only anomaly seen more frequently was holoprosencephaly.

The mechanisms that link obesity and congenital anomaly are not fully understood. Several possible hypotheses have been suggested, one being the prevalence of undiagnosed type II diabetes or significant insulin resistance without frank glucose dysregulation. Epidemiological data from both the USA and Europe have suggested that 30–50% of adults with type II diabetes are undiagnosed. Some studies suggest that prepregnancy diagnosis of diabetes may permit appropriate intervention prior to conception and that obese women planning a pregnancy should be screened and offered a high-dose folic acid supplement. One could postulate that weight reduction and tight glycaemic control could help reduce the rates of congenital abnormality in this high-risk group.

Box 1

<table>
<thead>
<tr>
<th>Complications that are more prevalent among obese women before and during pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prepregnancy</td>
</tr>
<tr>
<td>Early pregnancy</td>
</tr>
<tr>
<td>Antenatal</td>
</tr>
<tr>
<td>Intrapartum</td>
</tr>
<tr>
<td>Postpartum</td>
</tr>
<tr>
<td>Fetal</td>
</tr>
</tbody>
</table>

© 2009 Royal College of Obstetricians and Gynaecologists
Ultrasound and obesity

Obstetric ultrasound is widely practised throughout the developed world. Initially, its major indications were pregnancy dating and detection of multiple pregnancy and fetal growth restriction. With improved resolution the detection of fetal anomaly has become possible. The limitations of obstetric ultrasound as a screening test are dictated by the expertise of the clinician, the quality of the equipment and the habits of the woman. By absorbing the associated energy, adipose tissue can significantly attenuate the ultrasound signal. Therefore, a high-frequency, higher-resolution signal would be more significantly absorbed at a lesser depth, sacrificing image quality and depth of field. A worrying consequence of maternal obesity, consequently, is the reduced sensitivity of ultrasound as a screening test for fetal anomaly. In 1990, Wolfe et al. examined the efficacy of scanning the obese pregnant population. They showed that scans performed on women with a BMI greater than the 90th centile during the second and third trimester had a 14.5% reduction in visualisation of organs compared with lean women. This reduction was most marked when visualising the fetal heart, umbilical cord and spine.

Hypertension

Independent of pregnancy, hypertensive disorders are more prevalent in obese women than in their lean counterparts. Elevated prepregnancy BMI is an independent risk factor for the development of pregnancy-induced hypertension. Even when the degree of excess body fat is moderate, the incidence of hypertension and pre-eclampsia is significantly higher in comparison with control patients. Most published work suggests a two- to three-fold increase in the risk of pre-eclampsia with a BMI >30. Waist circumference has also been reported to be a sensitive predictive marker of possible pregnancy hypertensive complications. Sattar et al. examined early pregnancy body composition data from 1142 pregnant women. Odds ratios were calculated for risk of hypertensive complications of pregnancy in association with a waist circumference >80 cm at <16 weeks of gestation. The risk of pregnancy-induced hypertension was approximately doubled (OR 1.8, 95% CI 1.1–2.9) and of pre-eclampsia tripled (OR 2.7, 95% CI 1.1–6.8) in association with central obesity.

O’Brien et al. identified 13 cohort studies, comprising nearly 1.4 million women. The risk of pre-eclampsia typically doubled with each 5–7 kg/m² increase in prepregnancy BMI. This relationship persisted in studies that excluded women with chronic hypertension, diabetes mellitus and multiple gestation, or after adjustment for other confounding factors. A recent systematic review by Cnossen et al. aimed to determine the accuracy of maternal BMI in predicting pre-eclampsia and to explore the clinical potential for selecting women for treatment with low-dose aspirin. A total of 36 studies, testing 1 699 073 pregnant women (60 584 with pre-eclampsia) were included. They found that among women with a BMI >35 as the only risk, the incidence of pre-eclampsia was only 3%, resulting in 714 women needing treatment to prevent one case of pre-eclampsia. When a woman with a BMI >35 also had other risk factors, however, such as primigravidity or diabetes, the risk was greatly elevated and the number needed to treat in order to prevent one case of pre-eclampsia was only 37. This is a very useful paper for clinical practice and it highlights the importance of holistic evaluation of risk at booking for antenatal care. Most studies within the literature conclude that pregnancies amongst the obese population should be considered high risk and appropriate antenatal care provided. The need for prepregnancy counselling and advice for this group of women is highlighted repeatedly.

The mechanism of effect

As stated, obesity is a risk factor for many maternal obstetric complications, including pre-eclampsia and gestational diabetes. The mechanisms involved are complex but one possible unifying hypothesis is that there may be a syndrome of insulin resistance, low-grade inflammation, dyslipidaemia and an alteration in systemic microvascular function. This metabolic and vascular derangement mirrors that of the metabolic syndrome observed among those with coronary heart disease and/or diabetes, particularly in later life. In a prospective study, Stewart et al. demonstrated that obese women have a pro-inflammatory phenotype, with impaired microvascular function, from early in pregnancy. In lean women, inflammatory features were acquired in later pregnancy. The excessive inflammatory burden seen in the obese pregnant woman may fuel this process, explaining some of the increased association of obesity with pre-eclampsia and gestational diabetes.

Gestational diabetes mellitus and obesity

Gestational diabetes mellitus affects about 5% of all pregnancies. In the NICE consultation document on diabetes and pregnancy, a BMI >30 is considered a risk factor for the development of gestational diabetes. The policy has changed from offering no screening for gestational diabetes mellitus to targeted screening in the healthy maternal population, using clinical risk factors (Box 2).

Striking data from a large prospective population-based Swedish study, which included 151 025 women, warns of the implications of interpregnancy weight gain. This study shows that

© 2009 Royal College of Obstetricians and Gynaecologists
if an increase in maternal BMI of 1–2 units occurs between pregnancies, the risk of gestational diabetes rises by 20–40%. If a woman weighs 63 kg and is 1.65 m tall (BMI 23) and gains 3 kg before her second pregnancy, her BMI rises by 1 unit and her risk of gestational diabetes rises by >30%. If she gains 6 kg and, therefore, becomes overweight (gaining 2 BMI units), her risk of gestational diabetes rises by 100%. If she becomes obese, her risk of gestational diabetes rises by 200%. Effective treatment of gestational diabetes does reduce the risk of macrosomia. Instrumental and operative delivery rates, however, are increased even in the absence of fetal macrosomia. Crowther et al. conducted a randomised clinical trial to determine whether treatment of women with gestational diabetes mellitus reduced the risk of perinatal complications. The rate of serious perinatal complications was significantly lower among the infants of subjects in the intervention group than among the infants of the women in the routine care group (1% versus 4%, \( P=0.01 \)).

If gestational diabetes mellitus is diagnosed, tight metabolic control should be achieved through diet and, when indicated, insulin therapy. Insulin therapy is required more often in obese women with gestational diabetes mellitus than in lean women. Treatment using insulin reduces maternal and fetal morbidity. Mothers who develop gestational diabetes have a 50% higher risk of developing diabetes during their lifetime and this risk may be greatest in obese women. For the obese individual with gestational diabetes, pregnancy offers an ideal opportunity to give them future lifestyle advice in terms of exercise and weight loss and, therefore, to reduce the potential for vascular disease in the long term.

**Intrapartum issues**

Obesity and diabetes are independently associated with adverse pregnancy outcomes. Rosenberg et al. undertook a large population-based study. Data were collected from the 1999, 2000 and 2001 New York City birth files for 329 988 singleton births, containing information on prepregnancy weight and antenatal weight gain. During pregnancy, obese women are at increased risk of several adverse perinatal outcomes, including anaesthetic, periorioperative and other maternal and fetal complications. Obese women have higher rates of induction of labour and failed induction (7.9% versus 10.3% versus 14.6% with increasing BMI). Caesarean section rates in nulliparous obese women are higher than in lean women (20.7% in the control group versus 33.8% in the obese group and 47.4% in the morbidly obese group; \( P > 0.01 \)). A higher rate of obstetric complications among obese women has been reported, including operative vaginal delivery (8.4% versus 11.4% and 17.3% with increasing BMI; \( P < 0.001 \)), shoulder dystocia (1% versus 1.8% and 1.9% with increasing BMI; \( P < 0.021 \)) and third/fourth-degree lacerations (26.3% versus 27.5% and 30.8% with increasing BMI; \( P < 0.001 \)) compared with the normal BMI group. The frequency of both elective (8.5% versus 4%) and emergency caesarean section (13.4% versus 7.8%) is almost doubled for very obese women compared with the normal BMI group. When other factors such as macrosomia, nulliparity, induction or diabetes were accounted for, maternal obesity was still found to influence the mode of delivery independently. In another study of 126 080 deliveries, after excluding women with diabetes and hypertensive disease, there was a three-fold increased risk of failure to progress in the first stage and almost a trebling of caesarean section rate from 10.8% to 27.8% (OR 3.2) among obese women when compared with lean.

From the anaesthetic perspective, the risks of failed epidurals, increased aspiration during general anaesthesia and difficulty with intubation are the most commonly cited complications. Increased rates of caesarean delivery, macrosomia, shoulder dystocia, difficulty obtaining peripheral intravenous access and inaccurate or difficult blood pressure monitoring are also reported. Common operative complications include loss of landmarks, making vascular access difficult, and increased risk of respiratory complications, such as aspiration and pneumonitis. Increased retention of lipid-soluble agents, increased drug distribution and more rapid desaturation have also been reported.

The anaesthetist plays an important role in preventing serious complications and must be aware of the many potential hazards. Extra vigilance is required to guide these women safely through the periorioperative period. There are very few trials in the literature on the use of epidural and spinal anaesthesia in the obese woman. Many case reports exist on the difficulty of technique and reductions in drug dosage requirements.

**Postpartum issues**

It is now recognised that adipose tissue produces a variety of bioactive peptides, collectively termed adipokines. Alteration of adipose tissue mass in

---

**Box 2 Criteria meriting antenatal screening for gestational diabetes**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &gt; 30</td>
<td>Previous gestational diabetes</td>
</tr>
<tr>
<td></td>
<td>Previous macrosomic baby ≥4.5 kg</td>
</tr>
<tr>
<td></td>
<td>Family history of diabetes (first-degree relative with type 1 diabetes)</td>
</tr>
</tbody>
</table>

Belonging to a high-risk ethnic group, including:

- South Asian (Indian, Pakistani, Bangladeshi)
- Black Caribbean
- South Asian (Indian, Pakistani, Bangladeshi)
- Chinese

[28] The frequency of both elective (8.5% versus 4%) and emergency caesarean section (13.4% versus 7.8%) is almost doubled for very obese women compared with the normal BMI group. When other factors such as macrosomia, nulliparity, induction or diabetes were accounted for, maternal obesity was still found to influence the mode of delivery independently. In another study of 126 080 deliveries, after excluding women with diabetes and hypertensive disease, there was a three-fold increased risk of failure to progress in the first stage and almost a trebling of caesarean section rate from 10.8% to 27.8% (OR 3.2) among obese women when compared with lean.

© 2009 Royal College of Obstetricians and Gynaecologists
obesity affects the production of most adipose-secreted factors; there is an increase in several adipokines. Increased levels of angiotensinogen have been implicated in hypertension; PAI-1 in impaired fibrinolysis; and acylation-stimulating protein, tumour necrosis factor-alpha, interleukin-6 and resistin in insulin resistance.\(^{39}\) Pregnancy is a prothrombotic state, secondary to an increase in activity of coagulation factors XII, X and VIII, as well as fibrinogen.\(^{29}\) In the puerperium, deep venous thrombosis, endometritis, postpartum haemorrhage, prolonged hospitalisation and wound infection and dehiscence are also seen with increased frequency in obese women.\(^{29}\)

The leading cause of maternal mortality remains venous thromboembolism and the postpartum period is the time of greatest risk, secondary to vascular damage at childbirth. The coagulation cascade is activated by inflammatory cytokines causing endothelial activation and this is further increased with obesity. Several studies have shown that obese patients have higher plasma concentrations of all prothrombotic factors (fibrinogen, von Willebrand factor [VWF] and factor VII), compared with non-obese controls, with a positive association with central fat.\(^{29}\) It has been proposed that the secretion of interleukin-6 by adipose tissue, combined with the actions of adipose tissue-expressed tumour necrosis factor-alpha in obesity, could underlie the association of insulin resistance with endothelial dysfunction, coagulopathy and coronary heart disease.\(^{41}\)

**Implications for the fetus of the obese mother**

**Short-term**

Lower Apgar scores have been reported in the neonates of obese mothers compared with those of lean mothers.\(^{15}\) Prepregnancy BMI is a strong positive predictor of birthweight. In fact, the odds ratio for an obese mother delivering a large-for-dates infant is 1.4–1.8.\(^{11}\) Macrosomia increases the risk of shoulder dystocia, birth injury and the incidence of low Apgar scores and perinatal death. A recent 3-year retrospective analysis\(^{40}\) examined the mode of delivery of infants weighing >4000 g. The incidence of caesarean section among the macrosomic group was 25.8%, compared with 13.1% (P<0.0001) for the general population during the study period.

Infants born to obese mothers are more likely to require admission to a neonatal intensive care unit (NICU). In a retrospective study carried out in France,\(^{41}\) the percentage of infants requiring admission to a NICU was 3.5 times higher when maternal obesity was present. The higher incidence of diabetes mellitus and gestational diabetes in the obese population may contribute to this effect, with an increased risk of neonatal admission to the NICU for glycaemic control. The increased incidence of macrosomia and consequent birth trauma may also contribute to increased rates of perinatal morbidity in the offspring of obese mothers.

One cohort study carried out in Denmark\(^{42}\) examined the relationship between maternal prepregnancy BMI and the risk of stillbirth and neonatal death. Maternal obesity was associated with almost a three-fold increased risk of stillbirth (OR 2.8, 95% CI 1.5–5.3) and neonatal death (OR 2.6, 95% CI 1.2–5.8) compared with women of normal weight. Adjustment for maternal cigarette smoking, alcohol and caffeine intake, maternal age, height, parity, gender of the child, years of schooling, working status and cohabitation with the partner did not change the conclusions, nor did exclusion of women with hypertensive disorders or diabetes mellitus. No single cause of death explained the higher mortality in children of obese women but more stillbirths were either unexplained intrauterine deaths or associated with feto-placental dysfunction among obese compared with normal weight women.\(^{42}\)

**Long-term**

Barker’s hypothesis\(^{45}\) describes a theory of intrauterine programming, which suggests that babies who are small at birth or during infancy, secondary to maternal starvation during pregnancy, have increased rates of cardiovascular disease and type 2 diabetes in adult life. Forsén et al.\(^{44}\) examined the association between maternal BMI and the risk of coronary heart disease in the next generation. Men whose mothers had a high BMI in pregnancy had an increased risk of coronary heart disease. The highest death rates were, therefore, in men who had a low birthweight and a low placental weight but whose mothers had a high BMI during pregnancy. The effects were large and highly significant. While undernutrition is uncommon in the developed world, obesity and cardiovascular disease are common. The direct effects of maternal obesity on fetal programming are under-researched. The concept of fetal programming being related to the quality of nutrition, rather than the quantity, needs to be addressed. One may hypothesise that, in addition to maternal malnutrition secondary to famine, malnutrition secondary to an inappropriate diet of highly processed, high-fat food lacking in essential vitamins and nutrients, i.e. the modern Western diet, may contribute to long-term adult ill health of offspring through fetal programming.

**Cost implications**

In 2000, a prospective study\(^{46}\) examined the cost of care of 435 women seen consecutively within their obstetric service. The average cost in terms of
anténatal care and duration of hospital stay was five times higher for women who had a higher prepregnancy BMI compared with normal weight controls and duration of hospital stay was 3.9 to 6.2-fold higher among the overweight mothers.

The overall financial burden of obesity on the National Health Service is difficult to determine. The implications of rising rates of maternal obesity for antenatal services include increased medicalisation of labour and delivery and greater pressure on neonatal services and antenatal and postnatal beds.

Conclusion and recommendations

It is essential that obstetricians have guidelines for management of the obese woman. Obesity is a risk factor for both gynaecological and obstetric complications. A multidisciplinary approach to management is necessary to decrease the risks of morbidity and mortality. There are a number of recommendations for clinical management prior to and during pregnancy:

• Provide prepregnancy counselling for morbidly obese women (in primary care/subfertility/ recurrent miscarriage/obstetric/diabetic clinics).
• Consider high doses of folic acid (5 mg).
• A healthy diet and exercise are important in management.
• Consider high doses of folic acid (5 mg).
• Provide an early booking visit to plan pregnancy management.
• Prescribe low-dose aspirin in the presence of additional clinical risk factors for pre-eclampsia.

This group of women requires both primary and secondary care intervention if we are to limit or even reverse the epidemic of obesity within Western society.

References


© 2009 Royal College of Obstetricians and Gynaecologists