The implications of obesity on pregnancy outcome

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Abstract

Obesity is considered by the World Health Organisation to be a disease and is defined as a condition of excess body fat to a degree where it causes impairment to the health of an individual.

The World Health Organisation uses the body mass index (BMI) (weight(kg)/height(m)^2) to define overweight and obesity. Overweight is defined as a BMI of 25 or more and obesity as a BMI of 30 or more.

The rate of obesity is increasing worldwide, in both economically rich and poor countries. In 2005, it was estimated that 23% of the adult population was overweight.

In addition to the increased prevalence of obesity in the general population, the proportion of pregnant women who are obese is rising. A retrospective study of over 619 000 births from 34 UK maternity units determined that first trimester maternal obesity significantly increased over time and had more than doubled from 7.6% to 15.6% in 19 years.

Obesity in pregnant women is associated with a number of issues including recurrent miscarriage, increased risk of gestational diabetes, impaired fetal growth and poor obstetric outcome. This review will focus on these obstetric challenges.

Keywords macrosomia and postpartum haemorrhage; obesity; pre-eclampsia; recurrent miscarriage; thromboembolism

Miscarriage

Many studies have shown a direct link between obesity and miscarriage both in spontaneous pregnancies and in women who have had IVF treatment. A meta-analysis by Metwally et al. explored whether high body mass index increased the risk of miscarriage after spontaneous and assisted conception and reported that women with a BMI of more than 25 had a higher risk of miscarriage regardless of whether the pregnancy was conceived spontaneously or through assisted conception. A strong association between obesity and recurrent miscarriage has also been reported.

The mechanism by which obesity increases the risk of miscarriage is unclear. Poor oocyte quality because of deranged ovarian function, especially in women with polycystic ovary syndrome, and consequent poor embryo quality has been suggested. Other postulated mechanisms include effects of obesity on endometrial function.

Management of obese women following miscarriages is challenging as there is no strong evidence to support the contention that weight loss will improve pregnancy outcomes, although one study reported that insulin sensitising agents such as metformin may reduce the risk of recurrent miscarriage in obese women with polycystic ovary syndrome.

Gestational diabetes

Approximately 7–14% of all pregnancies are complicated by gestational diabetes mellitus (GDM). GDM is defined as glucose intolerance with its onset (or first diagnosis) during pregnancy. GDM may persist following delivery; this may indicate that glucose intolerance antedated or began with the pregnancy.

As with obesity, the worldwide prevalence of GDM is increasing. A number of studies have shown an increased risk of GDM among overweight and obese women, and a meta-analysis by Chu et al. indicated that the unadjusted ORs of developing GDM were 2.14 (95% CI: 1.82–2.53), 3.56 (3.05–4.21), and 8.56 (5.07–16.04) among overweight, obese, and severely obese compared with normal-weight pregnant women respectively. Nevertheless, an increased BMI has been reported to have a low predictive value for GDM.

Obesity is considered to be an insulin resistant state, and thus accentuates the insulin resistance of normal pregnancy. Obese women with GDM are more likely to need insulin to achieve good glycaemic control, as compared to women with normal BMIs, and the use of insulin in these pregnant women is also associated with better pregnancy outcome. Obese women who achieved targeted levels of glycaemic control have been shown to have comparable pregnancy outcomes to normal weight and overweight women who were similarly treated with insulin. In contrast, whilst normal weight women treated with diet therapy who achieved targeted levels of glycaemic control had good outcomes, obese women treated with diet therapy who achieved targeted levels of glycaemic control nevertheless had a 2- to 3-fold higher risk for adverse pregnancy outcome. Women with GDM who failed to achieve glycaemic control had significantly higher adverse pregnancy outcomes than all maternal weight groups.

Pre-eclampsia

Pre-eclampsia is a common multiorgan complication in pregnancy, affecting approximately 5% of healthy nulliparous women. Pre-eclampsia is defined as hypertension that is diagnosed for the first time after 20 weeks of gestation (systolic blood pressure >140 mmHg and diastolic blood pressure >90 mmHg on two separate occasions at least 4 hours apart) with significant proteinuria (++ or more on urine dipstick test or more than 300 mg on a 24 hour collection). Multisystem complications of pre-eclampsia can include: renal, haematological, hepatic, neurological, pulmonary and fetal growth restriction (Box 1).

Population based studies have found that rates of pre-eclampsia increase with increasing BMI; 'super-obese' women have the highest incidence (up to 13.4%). A systematic review of controlled studies by Duckitt et al. examined risk factors for pre-eclampsia at the antenatal booking visit; the relative risk (RR) of

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Maternal and neonatal complications

Maternal complications

- Abruptio placentae (1–4%)
- Disseminated coagulopathy/HELLP syndrome (10–20%)
- Pulmonary oedema/aspiration (2–5%)
- Acute renal failure (1–5%)
- Eclampsia (<1%)
- Liver failure or haemorrhage (<1%)
- Stroke (rare)
- Death (rare)
- Long-term cardiovascular morbidity

Neonatal complications

- Preterm delivery (15–67%)
- Fetal growth restriction (10–25%)
- Hypoxia-neurologic injury (<1%)
- Perinatal death (1–2%)
- Long-term cardiovascular morbidity associated with low birthweight (fetal origin of adult disease)

Magnitude of risk depends on gestational age at time of diagnosis, delivery, severity of disease process, and presence of associated medical disorders.

Box 1

pre-eclampsia in women with a raised BMI before pregnancy was 2.47 (CI 1.66–3.67). Other risk factors identified in this study included previous history of pre-eclampsia, diabetes mellitus, nulliparity, multiple pregnancy, maternal age more than 40 and increased blood pressure at booking.

The mechanisms explaining the relationship between obesity and pre-eclampsia are complex and not fully understood. A number of hormonal and biochemical pathways have been implicated including insulin resistance, endothelial cell activation, dyslipidemia and elevated cytokines such as tumour necrosis factor. Different studies have shown that these hormonal and biochemical changes can be identified prior to pregnancy, in early pregnancy before the onset of pre-eclampsia, and months after delivery.

Women with increased BMI who develop pre-eclampsia should be offered a postnatal follow up appointment to ensure that their blood pressure is back to normal and also to offer counselling regarding weight loss.

Thromboembolism

Venous thromboembolism (VTE) is an important cause of maternal morbidity and mortality. Up until the last confidential enquiry into maternal and child health (CMACE) it was the leading direct cause of maternal death.

Obesity is one of the most important risk factors for developing venous thromboembolism in pregnancy. According to the UK obstetric surveillance system, between February 2005 and August 2006, there were 143 cases of confirmed pulmonary embolism in pregnant women. This represented an incidence of 12.6 per 100 000 maternities. Obesity was the second most common identified risk factor, although multiparty was the commonest risk factor. A case control study in Norway examined 268 cases of confirmed antenatal venous thromboembolism and found that the risk of venous thromboembolism was raised in women with a BMI ≥25 (a OR 1.8 CI 1.3–2.4), and this risk increased if there was associated immobility with an increased BMI (OR 62.3 CI 11.5–337.6).

In the most recently published confidential inquiry into maternal deaths and morbidity (EMBRRACE 2014) there were 26 maternal deaths per 100 000 maternities due to thromboembolism (rate 1.08, 95% confidence interval (0.71–1.59)).

Pregnancy alone is a risk factor for venous thromboembolism due to a hypercoagulability, venous stasis and endothelial damage. This risk is further increased if the pregnant woman is overweight or obese; obesity increases the hypercoagulability state of pregnancy by a more pronounced effect on clotting factors. Venous return is worse in obese patients due to adipose tissue deposition and immobility. Obesity also causes endothelial damage by decreasing the endothelial vasodilatory response.

All pregnant women should be assessed at their booking visit for risk factors of venous thromboembolism; every pregnant woman should have her BMI checked at the booking visit and repeated at 36 weeks of gestation.

The Royal College of Obstetricians and Gynaecologists has published a green top guideline "Reducing the risk of thrombosis and embolism in pregnancy and the puerperium". In this guideline, obesity has been identified as a moderate risk factor, however, its importance relates to the high prevalence of VTE within the obese population. The recommendations of this guideline include that:

- All women with class three obesity: BMI >40 should be considered for thromboprophylaxis with low molecular weight heparin for 7 days regardless of mode of delivery.
- All women who have had an emergency caesarean section with a BMI >30 should be considered for thromboprophylaxis with low molecular weight heparin for 7 days after delivery.
- All women with a BMI >30 and one other risk factor (Table 1) for venous thromboembolism should be considered for thromboprophylaxis with low molecular weight heparin for 7 days after delivery (Box 2).

Calculation of Treatment Dosage of LMWH by Early Pregnancy Weight

	Early pregnancy weight (kg)			
	<50	**50–69**	**70–89**	**>90**
Enoxaparin	40 mg bd[a]	60 mg bd[a]	80 mg bd[a]	100 mg bd[a]
Dalteparin	5000 IU bd[a]	6000 IU bd[a]	8000 IU bd[a]	10,000 IU bd[a]
Tinzaparin	175 U/kg once Daily (all weights)	175 U/kg once Daily (all weights)	175 U/kg once Daily (all weights)	175 U/kg once Daily (all weights)

The dose of low molecular weight heparin is weight dependent.
[a] bd = twice daily.

Source: RCOG Guideline.

Table 1