

Gynaecol Perinatol 2015;24(3):89–98

School of Medicine, University of Zagreb, Clinical Department of Gynecology and Obstetric,
Zagreb University Hospital Center, Zagreb, Croatia

PREGNANCY, DELIVERY AND PUERPERIUM IN OBESE WOMEN

Marina Ivanišević, Nina Kosi, Josip Đelmiš, Josip Juras

Review article

Key words: obesity, pregnancy, delivery, perinatal care, maternal complications, fetal complications

SUMMARY. Obesity affects mental, physical and emotional health, increases the prevalence of hypertension, diabetes, sexual dysfunction and cardiovascular disease, and reduces the quality of life. Every woman with body mass index greater than 30 kg/m² is considered obese, which has negative sequels on her general and reproductive health. A higher prevalence of early habitual abortion, congenital anomalies, preterm delivery, preeclampsia, gestational diabetes, cesarean section, fetal growth retardation and thromboembolism has been reported in obese women. Obesity is associated with worse maternal and perinatal outcomes. Children born to obese mothers more frequently develop cardiovascular disease, type 2 diabetes and metabolic syndrome later in life. This review gives recommendations for preconception work-up, and antenatal, intrapartum and postpartum care of obese pregnant women and their newborns.

Introduction

Obesity develops when the intake of energy surpasses energy needs of the body, i.e. when the intake and production of fat exceeds the amount of fat oxidized in tissues. The body energy reserves in the form of carbohydrates are limited and strictly regulated, which, unfortunately, does not hold for fat reserves. A healthy person will gain weight if having plenty of food and is physically inactive. Human race is exposed to a pandemic of obesity due to changing lifestyle. The resulting obesity is the cause of many metabolic, cardiovascular, gastrointestinal, skeletal and articular diseases, as well as of some types of carcinoma. Excessive adipose tissue is mostly accumulated subcutaneously; however, fat is also deposited in other tissues such as parenchymatous organs. Depending on tissue type and distribution, adipose tissue differently influences development of insulin resistance. The abdominal type of obesity, which includes increased fat accumulation in the subcutaneous tissue in the trunk, abdominal cavity and to a lesser extent thoracic cavity, more frequently leads to metabolic and vascular disorders as part of the metabolic syndrome or insulin resistance syndrome.¹ It is explained by different expression of the enzymes involved in lipolysis, triglyceride synthesis and adiponec-

tin secretion in various adipose tissue segments.² Apart from adipose tissue, in severe obesity triglycerides are ectopically accumulated in all tissues, in particular the liver, muscle and pancreatic β -cells, where they express their lipotoxicity. They lead to hepatocyte dysfunction and β -cell dysfunction and apoptosis.³ Besides lipotoxicity, triglyceride deposits in the muscle and liver also cause insulin resistance.⁴

Obesity is a major medical problem in today's world, in both developed and developing countries. The share of obese adult women rises annually by 0.3%–0.6% in industrialized and developing countries alike. In spite of famine still present in great parts of the world, it is estimated that currently there are more than one billion obese people worldwide. In 95% of cases, the etiology of obesity remains unknown, and the majority of obese people suffer from this condition because they eat too much. When turning obese, other factors also become ever more pronounced (inadequate physical activity, altered metabolic and hormone mechanisms) and act so as to support its maintenance and progression. Obese individuals more frequently develop diabetes mellitus due to impaired insulin sensitivity of target organs and inability of the pancreas to respond to increased insulin requirements. These individuals have increased levels of blood cholesterol and triglycerides, which together

with elevated blood pressure leads to atherosclerosis. Because of hyperestrogenism, obese women have a higher prevalence of breast and endometrial carcinoma, oligomenorrhea, amenorrhea and anovulatory cycles. In morbidly obese, hypoxia and hypercapnia occur in sleep due to upper airway obstruction, which in turn may lead to polycythemia, pulmonary hypertension and chronic pulmonary heart. Great efforts have been invested to reduce the share of obese individuals because of the adverse health effects of obesity. Almost every fourth woman of generative age is overweight. In these women, pregnancy is burdened with obesity from the very beginning, thus increasing the risk of having macrosomic newborns.⁵ On the other hand, the risk of developing obesity in adulthood is greater in high birth weight infants.

In the World Health Organization (WHO) criteria, obesity is defined according to body mass index (BMI), which is calculated by the formula: $\text{BMI (kg/m}^2\text{)} = \text{body weight (kg)/body height (m}^2\text{)}$. Individuals with $\text{BMI} < 18.5 \text{ kg/m}^2$ are considered lean, whereas proportionate body built implies $\text{BMI } 18.5\text{--}24.9 \text{ kg/m}^2$. Individuals with $\text{BMI } 25.0\text{--}29.9 \text{ kg/m}^2$ are overweight and those with $\text{BMI} > 30.0 \text{ kg/m}^2$ are obese. There are three degrees of obesity: $\text{BMI } 30.0\text{--}34.9$ (first degree), $\text{BMI } 35.0\text{--}39.9$ (second degree) and $\text{BMI} \geq 40$ (third degree or extreme obesity) (Table 1). The advantage of BMI is ease of calculation, while its drawback is the inability to differentiate obesity and high muscle mass as the cause of high body weight. BMI correlates well with mortality, so that the risk of premature death is low in individuals with $\text{BMI } 20\text{--}25 \text{ kg/m}^2$, but is high in those with $\text{BMI} > 25 \text{ kg/m}^2$ and in particular in those with $\text{BMI} > 30 \text{ kg/m}^2$.

Table 1. Body mass index (BMI) levels and risk of health problems⁶

Underweight	$\text{BMI} < 18.5 \text{ kg/m}^2$	Risk increased
Normal weight	$\text{BMI } 1.85\text{--}24.9 \text{ kg/m}^2$	Lowest risk
Overweight	$\text{BMI} \geq 25\text{--}29.9 \text{ kg/m}^2$	Risk increased
Obesity	$\text{BMI} \geq 30 \text{ kg/m}^2$	
First-degree obesity	$\text{BMI } 30.34.9 \text{ kg/m}^2$	High risk
Second-degree obesity	$\text{BMI } 35\text{--}39.9 \text{ kg/m}^2$	Very high risk
Third-degree obesity (extreme obesity)	$\text{BMI} \geq 40 \text{ kg/m}^2$	Extremely high risk

In the United Kingdom and the USA, more than 50% of women of reproductive age have BMI greater than 25 kg/m^2 , with a 60% increase recorded during the 1990–2004 period.⁶ In Germany, a 0.39% annual increase in the prevalence of obesity has been recorded over the past two decades, when it was 22.5%. In 2007, Germany had the highest number of obese individuals in Europe.⁷ However, in comparison to Germany, the share of obese individuals is higher in the United Kingdom, Greece and East European countries. Surprisingly, in spite of the traditionally healthy dietary habits, this unfavorable trend has also been recorded in Mediterranean countries, where the prevalence of obesity was low and constant in 1980, since when it has been

abruptly increasing, currently reaching 30% of the population of women and children.

General health

Obesity does not only influence reproductive health of women, since the association of overweight with higher insulin resistance, diabetes mellitus type 2, hepatic dysfunction, cardiovascular disease and metabolic syndrome is well known.⁸ Metabolic syndrome that includes insulin resistance, obesity, dyslipidemia and hypertension has been ever more frequently diagnosed. According to many published studies, the prevalence of obesity varies depending on the study population and the syndrome definition used. General prevalence is around 22% and has been definitely confirmed to depend on age groups. In recent years, along with body mass increase, a rise in the general prevalence of metabolic syndrome and its development at an ever younger age has been recorded; it has been estimated to be diagnosed in 9% of children aged > 12 . Besides age, other risk factors for metabolic syndrome development are body weight increase, ethnicity, postmenopausal period, smoking, poverty, carbohydrate rich diet and physical inactivity. The pathophysiology of metabolic syndrome is very complex and only partially clarified. Insulin resistance and abdominal and visceral type of obesity are considered as the basic pathophysiological mechanism of metabolic syndrome (Table 2). Metabolic syndrome has been associated with the onset of various other clinical entities such as diabetes mellitus, dyslipidemia, hypertension, visceral obesity, nonalcoholic fatty liver, polycystic ovary syndrome (PCOS), some malignant diseases, coagulation and fibrinolysis disorders, and inflammation.

Pregnancy is a specific metabolic-endocrinologic condition. In pregnancy, virtually all the symptoms related to metabolic syndrome are worsened, e.g. increase in insulin resistance, BMI increase, elevated concentrations of prothrombotic and proinflammatory factors, etc.

Table 2. Definitions of ‘metabolic syndrome’ in women (International Diabetes Federation, 2005) (9)

Increased waist circumference
• $\geq 80 \text{ cm}$ for women of European origin
Plus at least 2 of the following symptoms:
• therapy with antihypertensive agents and/or systolic blood pressure $\geq 130 \text{ mm Hg}$ and/or diastolic blood pressure $\geq 85 \text{ mm Hg}$
• therapy for elevated triglycerides and/or serum triglycerides $\geq 1.7 \text{ mmol/L}$
• therapy for decreased HDL cholesterol and/or HDL cholesterol $< 1.3 \text{ mmol/L}$
• fasting plasma glucose $\geq 5.6 \text{ mmol/L}$ or previously diagnosed diabetes mellitus type 2

Reproductive function is additionally aggravated, indirectly and by the above mentioned complications, by the ever older age at childbirth and the increasing prevalence of obesity in ever younger women.

Fertility

Reduced fertility in obese women has long been described. Anovulation is two to three times more common in obese women, which is explained by the increased peripheral insulin resistance and similar pathophysiologic mechanisms associated with hyperandrogenism and/or PCOS. PCOS is frequently associated with obesity and reduced fertility. Increased insulin resistance interferes with normal oocyte development. Weight loss and metformin therapy reduce insulin resistance and increase the likelihood of pregnancy.¹⁰ The rate of spontaneous pregnancy is also reduced in obese women with normal ovulation.¹¹

The outcome of *in vitro* fertilization (IVF) is also worse in obese women due to poorer oocyte and endometrium quality. Rittenberg *et al.* analyzed 33 studies reporting results on 48,000 IVF intracytoplasmic sperm injection (ICSI) in overweight women (BMI ≥ 25 kg/m²) and found a significantly lower prevalence of pregnancy (relative risk, RR=0.90) and live births (RR=0.84), and a significantly higher prevalence of spontaneous abortion (RR=1.31) as compared to normal-weight women (BMI < 25 kg/m²). Successful performance of IVF procedures was also reduced in obese women. The prevalence of pregnancy decreases with BMI increase. The probability of live births following IVF is lower in obese women as compared with normal-weight women.¹³

Preconception work-up in obese women

During follow up of pregnancy, delivery and puerperium in obese women, physicians are faced with numerous problems that need to be solved to achieve favorable perinatal outcome and prevent health deterioration of the obese pregnant women. Preconception work-up in obese women should include exact body height and body weight measurement and BMI calculation. Preconception is the ideal period for intervention for body weight loss and pregnancy outcome improvement in obese women. Obesity can be easily diagnosed before pregnancy or on initial examination. Such a timely diagnosis will allow enough time to plan the activities before and during pregnancy. In ideal circumstances, obese women should undergo preconception endocrinologic and metabolic work-up, along with lifestyle modifications in favor of their own and their future offspring health. This very motivation should be used to drive lifestyle changes that may otherwise present great challenge. These women should be encouraged to reduce BMI below 25 kg/m² or at least below 30 kg/m²; should be informed on the risks their obesity will probably entail during gestation; should be immediately advised on healthy dietary habits, programs for obese pregnant women and appropriate weight gain; inform them on health risks and potential health complications such as cardiac disease, hypertension, diabetes mellitus and obstructive sleep apnea. They should also receive explanation of the increased risk of fetal congenital anomalies and be warned of the methods of screening.

It appears reasonable to consult anesthesiologists in advance and point to the higher risk of cesarean section and the procedure related complications, as well as of the reduced likelihood of successful vaginal delivery following previous cesarean section. Appropriate prophylaxis should also be taken in consideration due to the greater risk of deep vein thrombosis.

Table 3. Preconception work-up in obese women

- Obese women should be advised on the importance of pregnancy planning, as well as on losing weight prior to pregnancy in order to reduce the prevalence of spontaneous abortion, congenital malformations, neonatal macrosomia and neonatal complications.
- Obese women should reach ideal body weight of < 25 kg/m² or at least < 30 kg/m² before pregnancy.
- Anovulation in obese women, which occurred due to excessive accumulation of adipose tissue, can be solved by healthy diet and physical activity. Adipose tissue reduction results in normalization of the adiponectin, leptin and insulin levels, thus enabling normal ovulatory function.
- Obese women should undergo the following laboratory work-up: oral glucose tolerance test (OGTT), thyroid-stimulating hormone (TSH), triglycerides (TG), free fatty acids (FFA), L-lactate dehydrogenase (LDH), high-density lipoprotein (HDL), liver function tests and creatinine.
- Obese women frequently suffer from hypertension and cardiac disease, therefore examination by nephrologist and cardiologist is recommended.
- Obese women take statins for hyperlipidemia and should stop taking them prior to planning pregnancy because of the proven teratogenic effects of these drugs.
- Obese women should receive instructions on gestational weight gain, diet and healthy food.
- Obese women should be explained that they are at an increased risk of cardiac and pulmonary disease, gestational hypertension/preeclampsia, gestational diabetes and obstructive sleep apnea.
- Regular daily physical activity is advised prior to planning pregnancy, as well as during pregnancy because it reduces the risk of complications mentioned above.
- Obese women should take folic acid (5 mg) for months before planning pregnancy because of the increased risk of congenital malformations.
- Obese women should be aware of the increased risk of thromboembolic disease during pregnancy and puerperium.

Pregnancy

Women may be overweight at the time of conception or may have high gestational weight gain, which results in obesity. Antepartum, intrapartum and postpartum complications are more common in such pregnancies. Frequent antepartum complications are spontaneous abortion, premature delivery, gestational hypertension, preeclampsia, gestational diabetes and urinary infections; intrapartum complications include those related to umbilical cord, meconium stained amniotic fluid and prolonged labor second stage; and postpartum complications are hemorrhage, puerperal infection and thromboembolism. Women with pre-pregnancy overweight more frequently have macrosomic children, which increases the use of oxytocin, as well as labor termination by operative vaginal procedure and cesarean section. Perinatal mortality is higher in neonates born to obese women, which is related to premature delivery and twin pregnancy. However, great gestational weight gain in women with high pre-pregnancy BMI can lead to the

higher rate of low birth weight infants. Children born to obese mothers more frequently suffer from major congenital malformations. Neural tube defects and other anomalies of the central nervous system, great blood vessel anomalies and anterior abdominal wall defects are more frequently found in children born to extremely obese women. Women with high gestational weight gain enter subsequent pregnancy with higher body weight. In obese women, delivery is more frequently terminated by cesarean section as compared to women with normal BMI. There is evidence for obesity as a risk factor for maternal mortality.¹⁴

Table 4. Antenatal care of obese women

- Intensive antenatal care of obese women is recommended. Follow up should be initiated before 10th week of gestation.
- Regular body height and body weight measurement and BMI calculation. In obese women, gestational weight gain of 4–9 kg is recommended (15).
- Dietary and healthy nutrition and physical activity in pregnancy.
- OGTT according to IADPSG criteria (16). Obesity is a major risk factor for gestational diabetes.
- Follow up by cardiologist (higher prevalence of ischemic heart disease).
- Follow up by anesthesiologist (difficulties on regional anesthesia).
- Thromboembolic prophylaxis in women with BMI >40. It should be initiated at the beginning of gestation and continued throughout gestation and for two weeks postpartum (body weight 91–130 kg: Clexan 0.8 mL or Fragmin 7000 units; body weight 131–170 kg: Clexan 1.0 mL or Fragmin 9000 units). Mobilization early postpartum.
- Obese women are more prone to preeclampsia. Additional risk factors include first pregnancy, preeclampsia in previous pregnancy, family history of preeclampsia, and multiple pregnancy.
- Frequent clinical and ultrasound (US) examinations in pregnant women with BMI >35 mg/m².

Table 5. Recommended gestational weight gain (GWG) according to body mass index (BMI) (15)

Group of women	BMI (kg/m ²)	Recommended GWG (kg)	Recommended GWG in 2 nd and 3 rd trimester (kg/week)
Underweight	<18.5	12–18	1–1.3
Normal weight	18.5–24.9	11–15	0.8–1
Overweight	25–29.9	6–11	0.5–0.7
Obese (all subgroups)	≥30	4–9	0.4–0.6

Gestational weight gain in obese women and perinatal outcome

Revision of the previous recommendations of the US Institute of Medicine from 2009 suggests gestational weight gain of 4–9 kg for women with pre-pregnancy BMI >30 kg/m², which differs considerably from the earlier recommendation of the same institution where gestational weight gain of 7 kg was considered optimal. In obese women, pregnancy is expected to result in greater than expected gestational weight gain, thus potentiating most of the risks associated with these pregnancies. Lower gestational weight gain has been found to reduce the risk of macrosomia, cesarean section and

preeclampsia but to increase the risk of fetal hypotrophy and premature delivery, along with increased perinatal mortality not related to diabetes mellitus type 2 or gestational diabetes. Considering the various types of obesity and metabolic disorders that may occur in particular women, it is no wonder that it is very difficult to identify absolute values that would be applicable to all women; therefore, an individualized approach is the most reasonable choice. Including obese pregnant women in various organized programs assisting them in regulating diet, physical activity and weight gain, offering them psychological support and adjusting pregnancy follow up according to their individual needs certainly is the optimal approach that warrants good results.

Table 6. Planning delivery in obese pregnant women

- All complications that may occur during delivery should be explained to obese pregnant women. Intrapartum complications are more common in obese women as compared to those with normal body weight.
- The slowing course of labor, shoulder dystocia, operative vaginal delivery and urgent cesarean section are more common in obese women.
- Cesarean section is more difficult to perform in obese women, while postoperative complications are more common as compared to women with normal body weight.
- Anesthesiology related complications are more common in obese pregnant women.
- Obese pregnant women that have previously had cesarean section (BMI >30) can decide on vaginal delivery upon giving their informed consent and having all the risk factors properly discussed.
- Obesity is a risk factor for unsuccessful vaginal delivery following previous cesarean section; morbid obesity (BMI >40) carries a high risk of uterine rupture and neonatal trauma during attempted vaginal delivery.
- Urgent cesarean section in obese women is associated with an increased risk of serious maternal morbidity due to anesthesia and intraoperative difficulties.
- An increased risk of postpartum bleeding.

Table 7. Care of obese parturients and newborns

- Obese women (BMI >35) should deliver at tertiary maternity wards.
- Increased risk of shoulder dystocia.
- Cesarean section in obese women requires a team of experienced and skilful gynecologists/obstetricians.
- Increased risk of postpartum bleeding and emergency medical interventions for life threatening complications.
- Neonates born to obese mothers are more frequently admitted to the Neonatal Intensive Care Unit (NICU).

Table 8. Care of obese puerperas

- Mobilization early after delivery is recommended.
- Thromboprophylaxis for 10 days postpartum irrespective of the method of labor termination.
- Elastic stockings during cesarean section and postpartum.
- Women should be motivated to breastfeed their infants.
- Counseling about healthy diet and physical activity.
- If gestational diabetes has been diagnosed in pregnancy, OGTT should be performed at six weeks postpartum and then once a year.

Spontaneous abortion

Spontaneous abortion is more common in obese women.¹⁷ Boots *et al.*¹⁸ analyzed six studies with a total of 28,538 obese women and found a 16.6% prevalence

of spontaneous abortion *versus* 10.7% in the group of normal-weight women (odds ratio, OR 1.31; 95% confidence interval, 95% CI 1.18–1.46). Spontaneous abortion is more common in women with PCOS and those with isolated insulin resistance. In their study, Lashen *et al.*¹⁹ included 1644 obese women and 3288 normal-weight women and recorded a significantly higher rate of spontaneous abortion in the former (OR 1.2 and 3.5; 95% CI 1.01–1.46; $P=0.04$). Most researchers conclude that obese women have a higher prevalence of spontaneous and habitual abortion as compared with normal-weight women.^{20,21}

Congenital anomalies

The prevalence of congenital anomalies in infants born to mothers with high pre-pregnancy BMI rises with the degree of maternal obesity.²² Comparison of obese women with normal-weight women revealed the former to have a higher prevalence of congenital malformations, as follows: neural tube defect (OR 1.87; 95% CI 1.62–2.15); spina bifida (OR 2.24; 95% CI 1.86–2.69); cardiovascular malformations (OR 1.30; 95% CI 1.12–1.51); atrial and ventricular septal defects (OR 1.20; 95% CI 1.09–1.31); cleft palate (OR 1.23; 95% CI 1.03–1.47); cleft lip (OR 1.20; 95% CI 1.03–1.40); anorectal atresia (OR 1.48; 95% CI 1.12–1.97); hydrocephalus (OR 1.68; 95% CI 1.19–2.36); and extremity malformations (OR 1.34; 95% CI 1.03–1.73).

The highest risk increase refers to heart and central nervous system anomalies. The calculated relative risk (RR) for all anomalies of the neural tube development is 1.87 (95% CI 1.62–2.15), and isolated RR is 2.24 (95% CI 1.86–2.69) for spina bifida, 1.39 (95% CI 1.03–1.87) for anencephaly, and 1.30 (95% CI 1.12–1.51) for heart defects. An increased prevalence of hypospadias (RR 1.33; 95% CI 1.03–1.72), omphalocele (RR 1.63; 95% CI 1.07–2.47), hydrocephalus (RR 3.69; 95% CI 1.19–11.44), cleft lip and cleft palate (RR 3.02; 95% CI 1.1–6.0) and anorectal atresia (RR 1.48; 95% CI 1.12–1.97) has also been reported.²² The reason for the more frequent occurrence of congenital anomalies in obese women in part lies in inappropriate diet of these pregnant women; being aware of their obesity and motivated by pregnancy, they frequently start radical diets; in addition, there is diabetes and its complications, with a note that 30% of diabetes cases remain unrecognized in the population (although exclusion of diabetes mellitus does not mean risk elimination); low serum folate level in the obese and unknown supplementary folic acid dosage according to the degree of obesity and difficult US visualization of fetus in obese women, which reflects on the rate of antenatal detection of anomalies. Heart defects are recognized in 18.7% and 37.3% and neural tube anomalies in 29.5% and 42.8% of normal pre-pregnancy BMI and excess pre-pregnancy BMI women, respectively.²³

Premature delivery

Pre-pregnancy obesity is a risk factor for premature delivery.^{23,24} Premature delivery can be spontaneous or

elective. Preeclampsia is a frequent complication in obese women and a common indication for elective premature delivery. The risk of premature delivery increases with BMI increase. The rate of premature delivery is 0.17% in women with normal BMI (BMI 18.5–<25); 0.21% in women with BMI 25–<30; 0.27% in women with BMI 30–<35; 0.35% in women with BMI 35–<40; and 0.52% in women with BMI >40. Cnattingius *et al.*²⁵ compared the rate of premature delivery between obese and normal-weight women, with the following results: BMI 25–<30 (0.21%; OR 1.26; 95% CI 1.15–1.37); BMI 30–<35 (0.27%; OR 1.58; 95% CI 1.39–1.79); BMI 35–<40 (0.35%; OR 2.01; 95% CI 1.66–2.45); and BMI ≥ 40 (0.52%; OR 2.99; 95% CI 2.28–3.92). Based on the results obtained, the authors conclude that the risk of spontaneous premature delivery increases with maternal BMI increase. Overweight and obesity are associated with a higher prevalence of chorioamnionitis in premature delivery. Obese pregnant women are at a higher risk of genital and urinary infections, which has been identified as a risk factor for chorioamnionitis.^{26,27} The high proportion of elective prematurity due to maternal reasons in obese women carried most of the risk of premature delivery in almost all studies (RR 1.3; 95% CI 1.23–1.37).²⁶

Hypertensive disease in pregnancy and preeclampsia

Association of preeclampsia and obesity has been demonstrated in a number of studies, yielding a two- to threefold greater risk.²⁸ It can in part be explained by the considerably higher proportion of pregnant women with chronic hypertension in the population of obese women of reproductive age (12% *vs.* 3%) (28). In their meta-analysis of 13 cohort studies, O'Brien *et al.* found each pre-pregnancy 0.6 kg/m² BMI increase to nearly double the risk of subsequent preeclampsia. Weight loss or weight gain in-between pregnancies will reduce or increase the risk of hypertension in overweight and obese women.²⁸ Adipose tissue distribution is of great importance in obese women, as the visceral type of obesity carries a considerably greater risk than other types of obesity. In women with pre-pregnancy waist circumference >80 cm, the rate of isolated hypertension in pregnancy is twofold (OR 1.8; 95% CI 1.1–2.9) and of preeclampsia threefold greater (OR 2.7; 95% CI 1.1–6.8).²⁹ Abdollahi *et al.* report on waist circumference to be superior to BMI in predicting subsequent development of preeclampsia.³⁰ Pregnant women with preeclampsia have elevated levels of insulin, lipid and coagulation factors.

Dyslipidemia

Elevated blood lipid level is a common finding in pregnant women. Insulin has an important role in the glucose and lipid metabolism. Lipid concentration increases with the progression of pregnancy. In obese pregnant women and pregnant women with gestational

diabetes, elevation of blood lipid concentration is even more pronounced.³¹ In obese pregnant women, elevated blood lipid levels lead to increased fat deposits in tissues, increased secretion of inflammation proteins and insulin resistance.

Thromboembolism

Pregnancy as a procoagulatory state increases five-fold the risk of deep vein thrombosis and its complications. The risk is additionally increased twofold by obesity due to higher coagulation factor concentrations.

Diabetes mellitus type 2 and gestational diabetes

Obesity is the most common risk factor for insulin resistance. In pregnancy, insulin sensitivity is decreased by 50%–60%. The prevalence of gestational diabetes is increased in pre-pregnancy overweight or obese women. The risk of gestational diabetes increases with BMI increase. For example, OR for developing gestational diabetes is 1.97 for overweight women, 3.01 for obese women, and 5.55 for morbidly obese women.³² Increase in adipose tissue, visceral obesity in particular, is a major factor for developing insulin resistance. Obesity is considered as the greatest risk factor for developing metabolic syndrome, which is found in 4.6% of women with BMI 18.5–25 kg/m² and 60% of obese women. Therefore, it is no surprise that the presence of gestational diabetes is tenfold higher in obstetric history of obese women. The expected incidence of gestational diabetes in obese women varies among different settings, exceeding 25% with BMI >35 kg/m². Each 1 kg/m² BMI rise increases the rate of gestational diabetes by 0.92%; irrespective of the particular setting specificities, the rate of gestational diabetes in obese women is expected to be twofold to fivefold prevalence recorded in the general population.³³ Considering the higher subsequent rates of diabetes mellitus type 2 in women with gestational diabetes and their association with obesity, the role of post-puerperium endocrinologic work-up in these women is of utmost importance. Weight loss and healthy lifestyle help prevent diabetes mellitus type 2 development and reduce the prevalence of gestational diabetes. However, increased gestational weight gain results in an increased prevalence of gestational diabetes in obese women.

Fetal growth

Association of maternal obesity and fetal growth has long been recognized. As early as 1996, Brown *et al.* established correlation of pre-pregnancy waist and hip circumference with neonatal birth characteristics, calculated as follows: each 0.1 increase in this value increased neonatal birth weight by 120 g, birth length by 0.5 cm, and cranial circumference by 0.3 cm.³³ Although some studies define pre-pregnancy obesity as a risk factor for fetal hypotrophy and/or intrauterine growth re-

tardation, in the majority of cases these results did not reach statistical significance after elimination of the co-factors (chronic hypertension and preeclampsia). The higher prevalence of growth retardation in fetal deaths among obese women cannot yet be explained but remains a fact that needs to be taken in consideration on antenatal care planning. Association of pre-pregnancy obesity and accelerated fetal growth has been demonstrated when used to estimate the occurrence of hypertrophy or macrosomia alike. The reported factor of correlation between pre-pregnancy BMI and neonatal birth weight is 0.20, while the likelihood of macrosomia (birth weight >4500 g) increases with the degree of obesity, as follows: RR 2.0 (95% CI 1.4–3.0) with BMI >30 kg/m² and RR 2.4 (95% CI 1.5–3.8) with BMI >35 kg/m².³⁴ Although increased pre-pregnancy peripheral insulin resistance and/or gestational diabetes are more common in obese women, still more than 80% of these women have normal glucose metabolism. Studies have shown that obesity and these disorders are independent variables of accelerated fetal growth with a potentiated synergistic effect, whereas the pre-pregnancy waist-to-hip ratio is the most potent primary factor for both fetal hypertrophy and macrosomia.

Cesarean section

The rate of cesarean section is on an increase in almost all studies of the effect of pre-pregnancy obesity on pregnancy outcome, with a RR slightly greater than two. Urgent cesarean section is generally described as a predominant component of the overall increase, unlike elective cesarean section where there is no significant difference. It is attributed to the more than twofold higher likelihood of breech presentation, threefold higher likelihood of intrapartum dystocia, expected accelerated fetal growth, and all other comorbidities accompanying pregnancy in obese women.

Long-term sequels in children born to obese mothers

Fetal growth and development in obese women do not only determine perinatal features but also entail long-term consequences. The higher prevalence of childhood and adolescence obesity in infants born to obese mothers as compared to those born to mothers with normal BMI is well known.^{34,35} This can in part be ascribed to genetic factors; however, knowing that fetuses of obese pregnant women develop increased peripheral insulin resistance already *in utero* attracts interest in the theory of the various adult endocrinologic and metabolic functions being programmed during fetal life. The prevalence of childhood obesity is not increased among children born to obese mothers with gestational diabetes and with birth weight <4000 g, and *vice versa*. The risk of developing metabolic syndrome and diabetes mellitus type 2 in adulthood is independent of birth weight and is increased in all children born to obese mothers. The prevalence of hypertension and car-

diovascular risk in adulthood are considerably higher in children born to obese mothers.

Perinatal and maternal mortality

In comparison to pre-pregnancy normal-weight women, the RR fetal death is significantly higher in obese women, i.e. 2.4–3.1. On a sample of 134,527 pre-pregnancy obese women, Salihu *et al.* recorded a 40% increase in fetal mortality with the risk increasing in parallel to maternal BMI increase.³⁶ As expected, maternal mortality is higher in obese pregnant women as compared with the general population. Lewis reports on 35% share of obese pregnant women in the overall maternal mortality and more than 50% share if indirect causes of death are added.¹⁴

Conclusion

In obese women, fertility is reduced and anovulation is twofold to threefold more common, which is explained by increased peripheral insulin resistance and hyperandrogenism and/or PCOS. The most common antepartum complications are spontaneous abortion, premature delivery, gestational hypertension, preeclampsia, gestational diabetes and urinary infections; intrapartum complications include umbilical cord complications, meconium stained amniotic fluid and prolonged labor second stage; and postpartum complications are hemorrhage, puerperal infection and thromboembolism. Pre-pregnancy overweight women more frequently have macrosomic children, which increases the rate labor termination by operative vaginal procedure and cesarean section. Perinatal mortality is higher in neonates born to obese mothers, which is related to premature delivery and twin pregnancy. Children born to obese mothers more frequently suffer from major congenital malformations. Neural tube defects and other anomalies of the central nervous system, great blood vessel anomalies and anterior abdominal wall defects are more frequently found in children born to extremely obese mothers. Obese women are exposed to a number of risks potentially associated with long-term sequels for both the mother and the child.

PREPORUKE ZA SKRB PRETILIH TRUDNICA

Prekonceptijska obrada pretelih trudnica

- Pretile žene treba savjetovati o važnosti planiranja trudnoće, a i da smršave prije same trudnoće kako bi se smanjila učestalost spontanijeh pobačaja, kongenitalnih malformacija, rađanja makrosomne djece i neonatalnih komplikacija.
- Pretile žene bi trebale dostići idealnu tjelesnu težinu od <25kg/m² ili barem <30kg/m² prije trudnoće.

- Anovulacija kod pretelih žena koja je nastala zbog prekomjernog nakupljanja masnog tkiva se može riješiti zdravom prehranom i tjelesnom aktivnošću. Smanjenjem količine masnog tkiva normalizira se razina adiponektina, leptina i inzulina, a što omogućava urednu ovulacijsku funkciju.
- Pretelim ženama treba učiniti OGTT, TSH, trigliceride (TG), slobodne masne kiseline (SMK), LDH, HDL, jetrene probe, kreatinin.
- Pretile žene često imaju hipertenziju i bolesti srca pa se preporuča pregled kod nefrologa i kardiologa.
- Pretile žene zbog hiperlipidemije uzimaju statine. Zbog dokazanog teratogenog djelovanja žene trebaju prestati uzimati statine prije planiranja trudnoće.
- Pretile žene trebaju dobiti upute o prirastu tjelesne težine tijekom trudnoće, prehrani i izboru zdrave hrane.
- Pretelim ženama treba objasniti da imaju povećan rizik za srčane i plućne bolesti, gestacijsku hipertenziju/ preeklampsiju, gestacijski dijabetes i opstruktivnu apneju za vrijeme spavanja.
- Preporuča se redovita dnevna tjelesna aktivnost prije planiranja trudnoće, a i tijekom trudnoće jer smanjuje rizike navedenih komplikacija.
- Pretile žene trebaju uzimati folnu kiselinu (5 mg) mjesec dana prije planirane trudnoće zbog povećanog rizika za nastanak kongenitalnih malformacija.
- Pretile žene trebaju znati za povećan rizik od tromboembolijske bolesti tijekom trudnoće i babinja.

Antenatalna skrb pretelih trudnica.

- Preporuča se intenzivna antenatalna skrb pretelih trudnica. Kontrolu započeti prije 10. tjedna trudnoće.
- Redovito mjerenje tjelesne visine i težine i izračunati BMI. Za pretile trudnice preporuča se prirast tjelesne težine do 4–9 kg.¹⁵
- Dijetalna i zdrava prehrana, tjelesna aktivnost tijekom trudnoće.
- Učiniti OGTT prema kriterijima IADPSG.¹⁶ Pretilost je važan rizični čimbenik za GDM.
- Kontrola kod kardiologa (češća je ishemijska bolest srca).
- Kontrola kod anesteziologa – poteškoće kod davanja regionalne anestezije.
- Tromboembolijska profilaksa kod trudnica s BMI >40. Započeti od početka trudnoće, nastaviti tijekom trudnoće i dva tjedna nakon porođaja (tjele-

sna težina 91–130 kg Clexan 0,8 ml ili Fragmin 7000 jed. tjelesna težina 131–170 Clexan 1,0 ml ili Fragmin 9000 jed. Nakon porođaja rano ustajanje.

- Povećana je sklonost za preeklampsiju kod pretelih trudnica. Dodatni rizični čimbenici su: prva trudnoća, u prethodnoj trudnoći preeklampsija, obiteljska anamneza za preeklampsiju, višeploodna trudnoća.
- Češći klinički i UZV pregledi kod trudnica s BMI>35 mg/m²

Preporuke za prirast tjelesne težine u trudnoći prema Indeksu tjelesne mase (BMI)¹⁵

Skupine trudnica	Indeks tjelesne mase (BMI)	Preporučeni prirast tjelesne težine (kg)	Preporučeni prirast tjelesne težine u drugom i trećem tromjesečju (kg/tjedno)
Neuhranjene	< 18,5	12–18	1–1,3
Normalne težine	18,5–24,9	11–15	0,8–1
Prekomjerne težine	25–29,9	6–11	0,5–0,7
Pretile (sve skupine)	≥30	4–9	0,4–0,6

Planiranje porođaja kod pretelih trudnica

- Pretelim trudnicama treba objasniti sve komplikacije koje mogu nastatati tijekom porođaja. Češće su intraportalne komplikacije pretelih trudnica u odnosu na one s normalnom tjelesnom težinom.
- Češće je usporeno napredovanje porođaja, distocija ramena i veća učestalost operativno vaginalnoga porođaja i hitnoga carskog reza.
- Carski rez kod pretelih trudnica je teže izvesti, a postoperacijske komplikacije su češće u odnosu na trudnice s normalnom tjelesnom težinom.
- Češće su anesteziološke komplikacije kod pretelih trudnica.

- Pretile trudnice koje su prethodno rodile carskim rezom (BMI>30) mogu odlučiti o vaginalnom rađanju nakon informiranog pristanka kada se rasprave svi rizični čimbenici.
- Pretilost je rizični čimbenik za neuspjeli vaginalni porođaj nakon prethodnog carskog reza, a patološka pretilost (BMI>40) nosi visoki rizik za rupturu uterusa za vrijeme pokušaja vaginalnog rađanja kao i traume novorođenčeta.
- Hitan carski rez kod pretelih trudnica/rodilja je združen s povećanim rizikom ozbiljnog materalnog morbiditeta zbog anestezije i poteškoća tijekom operacije.
- Povećan je rizik postpartalnog krvarenja.

Skrb pretelih rodilja i novorođenčadi

- Pretile trudnice (BMI>35) bi trebale rađati u rodilištima treće razine
- Povećan je rizik za distociju ramena
- Carski rez kod pretelih trudnica zahtjeva tim iskusnih i spretnih ginekologa/opstetričara
- Povećan rizik od postpartalnog krvarenja i hitne medicinske intervencije zbog životne ugroženosti
- Novorođenčad pretelih majki se češće primaju u JINL (Jedinica intenzivnog neonatalnog liječenja)

Skrb pretelih babinjača

- Preporuča se rano ustajanje nakon porođaja
- Tromboprofilaksa nakon porođaja kroz 10 dana bez obzira na način dovršenja trudnoće
- Elastične čarape za vrijeme carskog reza i nakon porođaja
- Motivirati babinjaču da doji svoje dijete
- Savjetovati dijetalnu prehranu i tjelesnu aktivnost
- Ako je u trudnoći dijagnosticiran gestacijski dijabetes učiniti OGTT šest tjedana nakon porođaja i jedanput godišnje

References

1. Garg A. Regional adiposity and insulin resistance. *J Clin Endocrinol Metab* 2004;89:4206–10.
2. Bruce CR, Hawley JA. Improvements in insulin resistance with aerobic exercise training: a lipocentric approach. *Med Sci Sports Exerc* 2004;36:1196–201.
3. Collantes R, Ong JP, Younossi ZM. Nonalcoholic fatty liver disease and the epidemic of obesity. *Cleveland Clin J Med* 2004;71:657–64.
4. Ferrannini E, Haffner SM, Mitchell BD, et al. Hyperinsulinaemia: the key feature of a cardiovascular and metabolic syndrome. *Diabetologia* 1991;34:416–22.

5. Rauger Martin R, Hyde MJ, Modi N. Maternal obesity and infant outcome. *Early Hum Dev* 2010;86:715–22.
6. Obesity: Preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser.* 2000;894:i.
7. Germans Are Fattest People in Europe, Study Shows. *Der Spiegel.* 19 April 2007.
8. Ferrada C, Molina M, Cid L. Relationship between gestational diabetes and metabolic syndrome. *Rev Med Child* 2007;135(12):1539–45.
9. International Diabetes Federations. *Diabetes Atlas.* 3rd edition, 2007.

10. Clark AM, Thornley B, Tomlinson L, *et al.* Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. *Hum Reprod* 1998; 13:1502.
 11. van der Steeg JW, Steures P, Eijkemans MJ, *et al.* Obesity affects spontaneous pregnancy chances in subfertile, ovulatory women. *Hum Reprod* 2008;23:324.
 12. Rittenberg V, Seshadri S, Sunkara SK, *et al.* Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. *Reprod Biomed Online* 2011; 23:421.
 13. Pasquali R, Patton L, Gambineri A. Obesity and infertility. *Curr Opin Endocrinol Diabetes Obes* 2007;14:482–7.
 14. Lewis G. Confidential Enquiry into Maternal and Child Health. Saving Mothers' Lives – Reviewing maternal deaths to make motherhood safer 2003–2005. London: CEMACH, 2007.
 15. Rasmussen KM, Catalano PM, Yaktine AL. New guidelines for weight gain during pregnancy: what obstetrician/gynecologists should know. *Curr Opin Obstet Gynecol* 2009;21(6): 521–6.
 16. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva Ad, Hod M, Kitzmiller JL, Lowe LP, McIntyre HD, Oats JJ, Omori Y, Schmidt MI. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010;33(3):676–82.
 17. Bellver J. Obesity and poor reproductive outcome: female and male body weight matter. *Fertil Steril* 2013;99:1558.
 18. Boots C, Stephenson MD. Does obesity increase the risk of miscarriage in spontaneous conception: a systematic review. *Semin Reprod Med* 2011;29:507–13.
 19. Lashen H, Fear K, Sturdee DW. Obesity is associated with increased risk of first trimester and recurrent miscarriage: matched case-control study. *Hum Reprod* 2004;19(7):1644–6.
 20. Metwally M, Ong KJ, Ledger WL, Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. *Fertil Steril* 2008;90:714.
 21. Usha Kiran TS, Hemmadi S, Bethel J, Evans J. Outcome of pregnancy in a woman with an increased body mass index. *BJOG* 2005;112:768–72.
 22. Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA* 2009;301(6):636–50.
 23. Nelson SM, Matthews P, Poston L. Maternal metabolism and obesity: modifiable determinants of pregnancy outcome. *Hum Reprod Update* 2010;16:255–75.
 24. Owens LA, O'Sullivan EP, Kirwan B, Avalos G, Gaffney G, Dunne F. ATLANTIC DIP Collaborators. ATLANTIC DIP: the impact of obesity on pregnancy outcome in glucose-tolerant women. *Diabetes Care* 2010;33:577–9.
 25. Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikström AK, Granath F. Maternal obesity and risk of preterm delivery. *JAMA*. 2013 Jun 12;309(22):2362–70. doi: 10.1001/jama.2013.6295.
 26. McDonald S, Han Z, Mulla S, Beyene J. Overweight and obesity in mothers and risk of preterm birth and low birth weight infants: systematic review and meta-analyses. *BMJ* 2010;341: c3428.
 27. Bhattacharya S, Campbell DM, Liston WA, Bhattacharya S. Effect of body mass index on pregnancy outcomes in nulliparous women delivering singleton babies. *BMC Public Health* 2007;7:168.
 28. O'Brien TE, Ray JG, Chan WS. Maternal body mass index and the risk of preeclampsia: a systematic overview. *Epidemiology* 2003;14:368–74.
 29. Yogev Y, Visser GH. Obesity, gestational diabetes and pregnancy outcome. *Semin Fetal Neonatal Med* 2009;14:77–84.
 30. Abdollahi M, Cushman M, Rosendaal FR. Obesity: risk of venous thrombosis and the interaction with coagulation factor levels and oral contraceptive use. *Thromb Haemost* 2003;89: 493–8.
 31. Catalano PM, Nizielski SE, Shao J, Preston L, Qiao L, Friedman JE. Downregulated IRS-1 and PPARgamma in obese women with gestational diabetes: relationship to FFA during pregnancy. *Am J Physiol Endocrinol Metab* 2002;282: E522–E533.114
 32. Torloni MR, Betran AP, Horta BL, *et al.* Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. *Obes Rev* 2009;10:194–203.
 33. Brown JE, Potter JD, Jacobs DR Jr, Kopher RA, Rourke MJ, Barosso GM, Hannan PJ, Schmid LA. Maternal waist-to-hip ratio as a predictor of newborn size: results of the Diana Project. *Epidemiology* 1996;7:62–6.
 34. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics* 2005;115: 290–6.
 35. Catalano PM, Presley L, Minium J, Haugel-de Mouzon S. Fetuses of obese mothers develop insulin resistance *in utero*. *Diabetes Care* 2009;32:1076–80.
 36. Salihi HM, Dunlop A, Hedayatzadeh M, Alio AP, Kirby RS. Extreme obesity and risk of stillbirth among black and white gravidas. *Obstet Gynecol* 2007;110:552–7.
- Adresa autora:* Prof. dr.sc. Marina Ivanišević, Medicinski fakultet Sveučilišta u Zagrebu, Klinika za ženske bolesti i porodaje KBC Zagreb, Petrova 13, 10000 Zagreb; *E-mail:* marina.ivanisevic@pronatal.hr
- Paper received:* March 19th 2016
- Paper accepted:* March 28th 2016

Medicinski fakultet Sveučilišta u Zagrebu,
Klinika za ženske bolesti i porode KBC-a Zagreb

TRUDNOĆA, POROĐAJ I BABINJE U PRETILIH ŽENA

Marina Ivanišević, Nina Kosi, Josip Đelmiš, Josip Juras

Pregledni članak

Ključne riječi: pretilost, trudnoća, porođaj, perinatalna skrb, majčine komplikacije, fetalne komplikacije

SAŽETAK. Pretilost utječe na psihičko, fizičko i emocionalno zdravlje, povećava učestalost hipertenzije, dijabetesa, seksualne disfunkcije, kardiovaskularnih bolesti i smanjuje kvalitetu života. Pretilom se smatra svaka žena s indeksom tjelesne mase većim od 30 kg/m², što ima negativne posljedice na opće i reproduktivno zdravlje. Među pretilim trudnicama opisana je veća učestalost ranih habitualnih pobačaja, prirodnih anomalija, prijevremenog porođaja, preeklampsije, gestacijskog dijabetesa, carskog reza, poremećaja fetalnog rasta i tromboembolijske bolesti. Pretilost je združena s lošijim majčnim i perinatalnim ishodom. U kasnijem životu djeca pretilih majki češće obolijevaju od kardiovaskularnih bolesti, dijabetesa tipa 2 i metaboličkog sindroma. U ovom preglednom članku autori daju preporuke za predkonceptijsku obradu, antenatalnu, intrapartalnu i postpartalnu skrb pretilih trudnica i skrb njihove novorođenčadi.