

How mother's obesity may affect the pregnancy and offspring

Sandra A. Radzicka-Mularczyk¹, Marek Pietryga¹, Jacek Brazert¹

Department of Gynecology, Obstetrics and Gynecologic Oncology, Division of Obstetrics and Women's Diseases, Poznan University of Medical Sciences, Poland

ABSTRACT

One of the main reasons for the epidemic of obesity, which has already influenced the economic condition of health system worldwide, is our modern lifestyle having an unbalanced calorie intake and insufficient physical activity. Maternal-fetal nourishment and metabolism are the mechanisms of fetal programming of obesity-adiposity and non-communicable diseases that have been most extensively investigated. A mother's obesity is related to adverse outcomes for both mother and baby. Maternal overnutrition is also associated with a higher risk of gestational diabetes, preterm birth, large-for-gestational-age babies, fetal defects, congenital anomalies, and perinatal death. Women with obesity should be encouraged to reduce their body mass index (BMI) prior to pregnancy, and to limit weight gain during pregnancy. Obstetric ultrasound imaging in pregnant women is negatively affected by abdominal adipose tissue, having an adverse influence on congenital anomaly detection rates and the estimation of fetal weight.

Key words: obesity; body mass index; BMI; gestational diabetes mellitus; GDM; pregnancy; glucose intolerance; folates; vitamin B; homocysteine

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INTRODUCTION

Obesity is a global health issue that may relate to metabolic syndrome as well as insulin resistance, type 2 diabetes, hypertension, dyslipidemia, nonalcoholic fatty liver disease, renal failure, and cardiovascular disease. Obesity is widespread globally and represents one of the most challenging public health problems due to its associated morbidity, mortality, and health care costs. The growing incidence of obesity, one of the causes of preventable death, can be seen in both developed and developing nations in recent years [1]. Obesity among women of reproductive age is already widespread worldwide [2]. According to WHO's Body mass index (BMI) classifications, overweight is defined as 25–29.9 kg/m², class I obesity is defined as 30.0–34.9 kg/m², class II obesity as 35.0–39.9 kg/m², and class III obesity as > 39.9 kg/m².

Obesity during pregnancy also increases the chances of spontaneous and recurrent miscarriages, nonoptimal ultrasound screening for fetal abnormalities, congenital heart and neural tube defects, wound infections, maternal thromboembolic and anaesthesia complications, depression, breastfeeding problems, gestational hypertensive disorders, gestational diabetes, preterm birth, and large for gestational age at birth [2]. The mechanisms of these outcomes include changes in maternal glucose and hormone levels,

altered gene expression, and fetal epigenetic modification. Gestational diabetes mellitus (GDM) is a common disorder that influences approximately 7–14% of pregnancies. GDM is defined as a state of glucose intolerance and hyperglycemia with onset during pregnancy [3]. The increasing global incidence of type 2 diabetes mellitus (T2DM), combined with increases in childhood and adolescent obesity, is a significant public health concern. Maternal hyperglycemia is proven to be a risk factor for overweight or obese offspring [4].

Adipose tissue as an active endocrine organ, when produced in excess, may dysregulate metabolic, vascular, and inflammatory pathways in organs during pregnancy, affecting obstetric outcomes. Although the direct cause of obesity is usually the person's lifestyle, it is more significant to consider how the varied individual risks of obesity are promoted by obesogenic environments [5].

FETAL PROGRAMMING

By its effect on the intrauterine fetal environment, maternal overnutrition has a significant and life-long impact on the health of the child and on offspring obesity. Maternal nutritional status, unbalanced metabolism, infection, stress, and environmental conditions all have a vital influence on fetal growth and programming. Hence, each of the

Corresponding author:

Sandra A. Radzicka-Mularczyk

Department of Gynecology, Obstetrics and Gynecologic Oncology, Division of Obstetrics and Women's Diseases, Poznan University of Medical Sciences, 33 Polna St, 60–535 Poznan, Poland
 e-mail: sandra.radzicka@gmail.com

periconceptual, *'in utero'*, and postnatal periods are crucial in programming the next generation's medical condition. Transgenerational transmission may commence *'in utero'*, and as a result of epigenetic changes, may result in long-lasting or temporal changes in metabolic programming [6, 7], which may in turn lead to adverse health problems in adult life [8]. Such can be a result of fetal exposure to hyperglycemia, hyperinsulinemia, hyperlipidemia, or inflammatory cytokines. Pregnant women with obesity have a greater risk of many maternal and perinatal complications, and the risk probability elevates with each increased degree of maternal obesity [9]. Excessive gestational weight gain in women who are already overweight or obese, accounts for one-quarter of pregnancy complications (*e.g.*, gestational hypertension, preeclampsia, gestational diabetes, and preterm birth) and almost one-third of large for gestational age children [10].

VITAMIN B12, FOLATES, HOMOCYSTEINE

The micronutrients vitamin B12 (B12) and folate are vital for the synthesis of DNA, protein, and lipids, and as such are associated with the fetal programming of obesity [11]. An essential part of this process is the conversion of homocysteine (Hcy) to methionine, for which B12 and folate are primary cofactors. Moreover, the mitochondrial conversion of methylmalonyl-CoA to succinyl-CoA depends on B12 as a coenzyme. When the enzyme is absent, accumulation of the former compound stops fatty acid oxidation because of promoting lipogenesis. Therefore, some scientists claim that low levels of B12 may be connected to adipose tissue dysfunction and complications linked with obesity [12]. Decreased levels of B12 during pregnancy influence maternal obesity, insulin resistance in the mother and fetus, and neonate lipid profiles [12, 13]. Research from India and UK indicates that vitamin B12 and folate concentrations during pregnancy are associated with obesity and insulin resistance in mother and offspring [12, 14]. It has also been proved that B12 deficiency during pregnancy is widespread, especially in women with obesity, is individually connected with GDM, and may be partly responsible for macrosomia [15]. According to some American studies, high folate consumption is associated with worsening clinical symptoms of vitamin B12 deficiency. Summing up, scientists conclude that vitamin B12 and folate should be considered together in assessing their influence on metabolic syndrome factors such as insulin resistance in obese patients [16]. Since there have been many studies on maternal consumption of carbohydrates and fats and their connection with developing GDM, it has been suggested that group B vitamins may be involved in the origination of glucose intolerance [17].

Homocysteine (Hcy) is an intermediate molecule of methionine metabolism whose concentrations are increased in the presence of folate and vitamin B12 deficiencies. In-

creased homocysteine levels are associated with insulin resistance. It has been speculated that elevated homocysteine concentrations impair the endothelial function in skeletal muscles, adipose tissue, and the liver, thus reducing insulin delivery to these insulin-sensitive organs [18]. It has been proven that both acute and chronic exposures to homocysteine results in detrimental effects on b-cell metabolism and insulin secretion [19].

OBESITY AND GESTATIONAL DIABETES MELLITUS

Obesity is closely correlated with the metabolic complication gestational diabetes mellitus (GDM) that may arise from changes in glucose regulation. In offspring, there is an association between increased BMI during childhood and adolescence and exposure to type 2 diabetes mellitus (T2DM) during pregnancy and gestational diabetes mellitus (GDM) [20, 21]. The HAPO Study showed there was a continuous correlation between maternal glucose levels during pregnancy and newborn adiposity outcomes [22]. According to the HAPO-FUS study, children exposed to increased levels of glucose *in utero* are more likely to develop childhood adiposity, including becoming overweight or obese. Glucose levels lower than those that are diagnostic of diabetes are associated with higher childhood adiposity; and this may have implications for long-term metabolic health [23]. Exposure to maternal gestational diabetes mellitus (GDM) during intrauterine life leads to increased fetal growth. In the PRE-OBE study, children born to obese mothers had significantly higher birth weights and waist circumferences while infants born of mothers with GDM had higher waist/height indices compared with the control group [24]. Some other studies have found that the intrauterine effects of GDM on offspring BMI are impaired when data is adjusted for pre-pregnancy maternal BMI [4, 25]. A few studies have reported that GDM is associated with higher levels of abdominal fat [26–28], suggesting that intrauterine exposure to diabetes may increase the risk for visceral adiposity, which is, in turn, linked to adverse health complications, including type 2 diabetes and cardiovascular disease [29].

OBESITY AND PREGNANCY COMPLICATIONS

Women with obesity are not only at increased risk for developing diabetes, preeclampsia, preterm delivery, thromboembolic disease, and macrosomia, and experiencing stillbirth, but also have an increased risk for labour induction failure. Moreover, obesity is also associated with both elective and emergency caesarean delivery, a risk that increases in correlation with increased maternal weight [30]. Goetzinger et al. [31], examined the extremes of abnormal fetal growth and found no connection with maternal BMI. According to Kritzer et al. [32], the percentage error of

estimated fetal weight (5.0–7.1%) was significantly lower than previously reported (16–20%). Obesity may also impair the visualization of fetal anatomy, with poor image quality making clinical interpretation difficult or impossible. Despite, technological advances, ultrasound imaging of obese patients remains challenging due to the adverse effects of adipose tissue on the penetration of sound waves [33]. Maternal obesity, even in the absence of gestational diabetes, is a potential risk factor for conditions such as neural tube defects, congenital heart defects, anorectal atresia, hydrocephaly, hypospadias, and limb reduction defects. Aksoy et al. [34], found a significantly higher percentage error higher on the BMI scale, and reported a greater risk of nonoptimal visualization when BMI (kg/m²) was above the 90th percentile. Thus, patients with a BMI higher on the scale had higher failure rates than those with a lower BMI. In contrast to the above, Field et al. [35], and Farrell et al. [36], found that the accuracy of clinical and sonographic estimated fetal weight (EFW) measurements was not affected by increasing maternal obesity. In the study by Dashe et al. [37], it was shown that visualizing fetal anatomic structures is limited by increased maternal BMI during the standard second-trimester ultrasound examination. The finding that maternal obesity reduces the quality of prenatal, obstetric ultrasonography has also been described by other researchers [38, 39].

OBSESITY IN PREGNANCY AND FETAL MACROSOMIA

Fetal macrosomia is defined as a birth weight of > 4,000 g and is associated with delivery complications such as maternal birth canal trauma, severe postpartum bleeding, shoulder dystocia, brachial plexus injury, fractures, and stillbirth due to perinatal asphyxia. The classification differs from a large-for-date newborn who is ≥ 90th or ≥ 95th centile for gestational age. Macrosomia occurs in up to 10% of deliveries and can be caused by genetic factors, maternal obesity or diabetes, or a fetal medical condition that accelerates fetal growth [40]. Nowadays, most screening strategies are based on cross-sectional evaluation of fetal size (abdominal circumference [AC] or fetal weight) during the third trimester. An accurate identification of excessive fetal weight leads to induction of labour for suspected fetal macrosomia and results in fewer birth complications without increasing cesarean section and instrumental delivery rates. There are studies about serial ultrasound measurement for early detection of LGA and macrosomia, but with inconsistent results [41]. There is an open-ended discussion in the literature regarding which sonographic EFW formula best evaluates fetal macrosomia. In 2010, Hart et al. [42], recommended a new formula for weight estimation of the macrosomic fetus based on fetal biometry and maternal weight, that improved macrosomia detection rates. Some other re-

searchers have used AFI to predict fetal macrosomia [43]; while others proved that a head circumference/AC ratio measuring < 0.95th percentile had the highest sensitivity (39.4%) and specificity (89.4%) followed by a fetal AC measuring > 90th percentile [44].

CONCLUSION

In conclusion, pregnancy outcomes are influenced by pre-pregnancy BMI. Maintaining a healthy pre-pregnancy BMI reduces the risks of delivering preterm, large for gestational age, and macrosomic infants. It is crucial to limit adverse maternal and fetal outcomes caused by maternal obesity. To prevent the growing number of pregnancies affected by GDM, particularly in high-risk groups, there is a need for obesity-prevention strategies that begin early in life. If early pregnancy B12 status is individually predictive of incident GDM, such findings could potentially offer simple interventions to improve the metabolic conditions of pregnant women and their children. With GDM on the rise, there is an urgent need for more cost-effective strategies to reduce the burden of maternal and offspring consequences. Women with obesity should be encouraged to lose weight before they get pregnant, and to limit their weight gain during pregnancy.

Conflict of interest

The authors declare no conflicts of interest.

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