# COMPLICATIONS OF PREGNANCY IN WOMEN WITH OBESITY

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Abstract. The prevalence of overweight and obesity during pregnancy is a serious problem in modern obstetrics as it is a clinically significant risk factor for women's health during and after childbirth and has long-term consequences. Women with a high body mass index often face conception problems early on and have a higher risk of serious gestational complications during pregnancy. Obesity can adversely affect fetal and neonatal development and have consequences for children throughout their lives. This article provides an overview of conditions and factors related to obesity during pregnancy. The review is relevant not only for obstetrician-gynecologists but also for professionals in other specialties providing care to women of reproductive age, as preventing long-term complications associated with obesity requires a comprehensive multisystem approach.

*Keywords*: gestational complications, pregnancy with obesity, BMI (body mass index), obesity, preeclampsia, GDM (gestational diabetes mellitus).

### Introduction

Over the past two decades, the prevalence of obesity among women of reproductive age in the United States has noticeably increased. According to the National Health and Nutrition Examination Survey (NHANES), the relative frequency of obesity among women aged 20 to 39 has increased by 33%, from 29.8% in 2001-2002 to 39.7% in 2017-2018. In 2020, only every other woman giving birth had a normal body mass index (BMI), while 26.7% were overweight, and 29.5% were obese. In England, the prevalence of overweight and obesity among women is 35% among those aged 16 to 24, increasing to 61% in the age group of 35 to 44. Epidemiological studies have shown the highest prevalence of overweight and obesity among women in the Pacific Island nations, the Caribbean basin, and the Middle East. Considering the global nature of the obesity problem among pregnant women, complicating gestation in 39 million cases annually, this issue poses a serious threat to various populations and the future generation on a global scale. On the Global North, maternal mortality rates are less than 1 per 10,000 births, but stillbirths and late intrauterine deaths range from 4 to 6 per 1000 births. The dynamic decrease in these rates is partly due to the implementation of new dietary control technologies among women of reproductive age. However, unfortunately, there are currently no well-developed plans for weight control during pregnancy and addressing the consequences of excess weight postpartum. Nevertheless, several scientific studies have shown that relatively simple dietary interventions can be effective in controlling excessive weight gain and reducing the risk of complications during pregnancy.

Major Inflammatory and Metabolic Changes

The major inflammatory and metabolic changes during pregnancy are associated with weight gain. This indicator is individual and depends on several factors. On one hand, the increase in mass occurs due to the development of the placenta, amniotic fluid, and fetal tissues. On the other hand, there is an increase in the woman's body water and blood volume necessary to maintain

placental perfusion. Additionally, continuous preparation of the mammary glands for breastfeeding occurs, the size of the uterus increases, and fat deposition in the body takes place.

It is known that chronic positive energy balance, found in women with increased body weight and obesity, leads to increased accumulation of triglycerides and hypertrophy, based on adipogenesis processes (hyperplasia and hypertrophy of adipocytes). A range of different cytokines, proteins, and signaling molecules released by adipose tissue, which have a wide impact on the metabolic and physiological functions of other organs, can also be considered as possible factors contributing to pregnancy complications development.

Development of obesity is associated with the emergence of chronic low-grade inflammation and the development of insulin resistance. This phenomenon affects the metabolism of glucose, lipids, and proteins in pregnant women. The reasons for changes in insulin resistance during pregnancy are not fully understood, but it is hypothesized that this condition is related to alterations in the levels of regulators such as human placental lactogen [4], placental growth hormone, placental-origin microRNAs [5], as well as a decrease in adiponectin levels and an increase in pro-inflammatory cytokine levels. Fortunately, there is rapid reduction in insulin resistance in the postpartum period, suggesting the placenta's role in its development [4].

Subfertility and Pregnancy Loss

Probable disruptions in the hypothalamic-pituitary-ovarian axis in women with obesity often lead to subfertility and spontaneous pregnancy loss in this patient category. Compared to the general population, obese women have a threefold higher risk of experiencing oligo-ovulation or anovulation [6], which is associated with menstrual function disorders and reduces the chances of conception [7], thereby increasing the risk of subfertility or infertility [8]. Obesity negatively impacts embryo nidation processes, hindering early pregnancy development, increasing miscarriage rates, and worsening outcomes of assisted reproductive technologies [8]. Typically, obese women require significantly higher doses of gonadotropins, experience more cycle cancellations, fewer and lower-quality retrieved oocytes, lower embryo transfer rates, and are at greater risk of preterm delivery [9].

Hypertensive Disorders of Pregnancy

For many years, hypertensive disorders of pregnancy, such as gestational hypertension and preeclampsia, have been among the most serious and prevalent causes of maternal morbidity and mortality. Numerous publications indicate that an elevated body mass index (BMI) is one of the main factors contributing to the development of hypertensive syndromes, especially among primiparous women. For instance, Chang K. J., Seow K. M., Chen K. H. showed that primiparous women with obesity had a 5-fold higher risk of developing gestational hypertension compared to women with normal BMI, while women with excess body weight had a 2.1-fold increased risk [10]. The risk of developing preeclampsia increases significantly with each 5-7 unit increase in BMI. Moreover, the risk of hypertension development also depends on the degree of obesity. In cases of obesity II or III degree, the risk increases 3-4 times compared to women with obesity of degree I. It is interesting to note that preeclampsia occurs in only 10% of obese women, which some researchers associate with the presence/absence of insulin resistance and the degree of systemic inflammation in each individual case [11].

It's important to note that metabolic and vascular changes in pregnant women with obesity and hypertensive disorders lay the foundation for the development of cardiovascular disease risks later in life. Hypertensive disorders in obese pregnant women can lead to negative consequences for the fetus, including growth restriction, oligohydramnios, premature placental abruption, preterm birth, and perinatal death, with the risk of these outcomes significantly elevated in this group of women [10].

Some researchers have expressed the opinion that combining dietary interventions with increased physical activity has a significant effect on preventing these pathological conditions in women during pregnancy [12]. For example, it has been shown that reducing the consumption of trans fats, increasing intake of foods containing high-quality long-chain polyunsaturated fatty acids, protein, fiber, as well as consuming carbohydrates with a low glycemic index, plays a significant role in reducing weight gain during pregnancy.

Gestational Diabetes (GDM) increases the risk of developing type 2 diabetes (T2D) and higher risks of renal, metabolic, and cardiovascular diseases for women in the postpartum period. GDM is associated with increased risks of gestational hypertension, preeclampsia, and cesarean section. The presence of GDM in mothers also adversely affects the development of newborns. Typically, these children have increased risks of macrosomia, neonatal hypoglycemia, and in severe cases, fetal demise [16].

GDM has a recurring nature, and the described risks for both mother and fetus can reach 41% to 69% with recurrent occurrences [17]. Some publications indicate that approximately 70% of women who have had GDM develop diabetes within 22-28 years after pregnancy [18].

Depression and Anxiety Disorders

Authors of two recent meta-analyses have identified statistically significant albeit small positive correlations between obesity and maternal depressive and anxiety disorders, occurring both during pregnancy and in the postpartum period. Although researchers have not yet explained the mechanisms underlying this association, proposed hypotheses include disruptions in the hypothalamic-pituitary-adrenal axis, immune regulation disturbances, feelings of dissatisfaction with body perception, experiences of stigma, and associated overeating [19]. The authors emphasize the role of stigma. Given that obesity-related stigma is widespread, obese women are more likely to report depressive symptoms, maladaptive eating behaviors, and stress. Therefore, published works also address the existence of a reverse causality link, as women with poor mental health find it challenging to control their weight.

Maternal obesity is associated with an increased risk of structural fetal anomalies, including congenital heart defects and various types of neural tube defects. Some studies have demonstrated an almost twofold increase in the risk of severe structural fetal anomalies in groups of women with increased body mass.

**Operative Delivery** 

At least three available meta-analyses in the literature have compared the risks of planned and emergency cesarean sections in women with obesity, with all studies showing a correlation between higher BMI and emergency cesarean section [14]. These meta-analyses also explain other possible factors associated with emergency operative delivery in women with obesity, such as slowed cervical dilation, comorbid organ diseases, the likelihood of shoulder dystocia, and excessive weight gain during pregnancy. All cited publications indicate that women with obesity are also at risk of complications related to anesthesia, postoperative wound complications, excessive blood loss, venous thromboembolism, postpartum endometritis, and unsuccessful subsequent trial of labor after cesarean section [20].

Postpartum Hemorrhage

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Two recent meta-analyses [14], [21] have found that compared to women with normal weight pregnancies, women with obesity have an increased risk of postpartum hemorrhage. The data from these studies document that the risk can be highest in women with a BMI over 35. Researchers speculate that the increased risk of bleeding may be related to the larger distribution volume of uterotonic drugs administered and technical difficulties in assessing the uterine fundus and performing measures to stop bleeding, such as bimanual massage.

**Gestational Diabetes** 

One of the common complications of obesity in women is gestational diabetes (GDM), which is diagnosed in 0.5-15% of pregnant women worldwide. A recent meta-analysis showed that the likelihood of developing gestational diabetes is 3-4 times higher in women with obesity compared to women with normal weight [13],[14]. It has been found that gestational diabetes is more prevalent among Latin American women, Black women, Native Americans, Asians, or Pacific Islanders [15]. This condition is characterized by hyperglycemia, which is first detected during pregnancy and usually resolves after childbirth. Insulin resistance, which underlies the pathology, increases in early pregnancy, while glucose intolerance and excessive fetal weight gain occur later in pregnancy. Existing insulin resistance due to excess weight in women can exacerbate insulin resistance during pregnancy, suppressing pancreatic beta-cell function and leading to hyperglycemia similar to the mechanisms of developing diabetes [1].

The pathogenesis of GDM has been linked to genetic predisposition and the influence of adverse environmental factors. However, excessive body weight and obesity before pregnancy are among the most significant modifiable predictors capable of influencing disease development.

Postoperative Infection

It has been proven that women with obesity in the postoperative postpartum period have a twofold increase in the risk of developing surgical wound infections. The results of a metaanalysis, including six studies assessing the risk and frequency of any type of postpartum infectious complications (including wounds, urinary tract infections, perineum infections, breast infections) in postpartum women, showed a significantly higher risk of infection in women with obesity compared to women of normal weight (odds ratio - 3.34; 95% CI - 2.74-4.06) [22].

Venous Thromboembolism

One of the serious complications of pregnancy in women with obesity is the development of venous thromboembolism, and the frequency of this complication is also increased in this patient population. In one study we found, it was shown that the risk of thromboembolism is four times higher among women with a body mass index (BMI) of 40 and above compared to women of normal weight. The authors of the study note that thromboembolism of major vessels in the postpartum period is less directly related to the BMI at the time of delivery than to the BMI dynamics during pregnancy. However, the authors conclude that weight gain of more than 22 kg during pregnancy and cesarean section contribute more significantly to the increased risk of venous thromboembolism [23].

## Conclusions

Obesity is a widely prevalent issue among women of reproductive age, and its scale continues to increase year by year, necessitating long-term and systemic approaches for correction. Elevated BMI and the presence of obesity during pregnancy are associated with a significant increase in the risk of adverse outcomes for the mother, fetus, and newborn. However, there is evidence that interventions such as healthy eating and physical exercise, implemented during

preconception preparation or early pregnancy stages, may contribute to minimizing excessive weight gain during pregnancy and reducing the likelihood of severe maternal and perinatal morbidity and mortality.

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