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Obstetrics & Gynecology International Journal

Review Article

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Placental alterations and maternal/neonatal breast cancer development: a review of the literature

Abstract

Placenta consists a temporary but highly active organ that plays a central role in fetal development and helps regulate the hormonal environment during pregnancy. In recent years, researchers have become increasingly interested in whether placental weight may be linked to breast cancer risk in both mothers and their children.

Placental weight is often considered an indirect indicator of placental function and efficiency, and several studies suggest that unusually high placental weight may reflect increased exposure to hormones and growth factors associated with breast cancer development.

This review examines current evidence on the relationship between placental weight and breast cancer risk, focusing on possible hormonal, epigenetic, and inflammatory mechanisms.

Higher placental weight has been associated with elevated levels of estrogen and insulin-like growth factor 1 (IGF-1), both of which are known to influence mammary gland development and carcinogenesis.

Findings from cohort and case-control studies are discussed together with the biological mechanisms that may explain these associations. Finally, the review considers the possible clinical implications of these findings and highlights directions for future research.

Keywords: placental weight, breast cancer, neonatal risk, maternal cancer, in utero exposure, estrogen, IGF-1, mammary gland

Volume 17 Issue 5 - 2026

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Received: September 05, 2026 | **Published:** September 17, 2026

Introduction

Breast cancer remains the most commonly diagnosed cancer among women worldwide, and its development is influenced by a combination of genetic, hormonal, environmental, and reproductive factors.[1] Over the past few years, increasing attention has been given to pregnancy-related influences on breast cancer risk. Among these, the placenta has emerged as an important area of interest because of its central role in regulating fetal growth and the hormonal environment during pregnancy.

Placental weight is routinely measured in obstetric practice and is often used as an indicator of placental growth, vascularization, and overall efficiency. Abnormally high or low placental weight may reflect altered intrauterine conditions such as maternal diabetes, hypoxia, or hormonal imbalance.[2] Since the placenta is also responsible for producing hormones including estrogens, progesterone, human placental lactogen (hPL), and insulin-like growth factor 1 (IGF-1), researchers have suggested that placental weight may indirectly reflect the hormonal exposure experienced by both the mother and the fetus during pregnancy.[3]

The developmental origins of health and disease (DOHaD) hypothesis proposes that exposures during fetal life can influence the risk of disease later in adulthood.[4] Within this framework, higher placental weight may indicate increased hormonal activity during pregnancy, which could potentially affect future breast cancer risk in female offspring. At the same time, prolonged exposure of the mother to pregnancy-related hormones may also influence her own long-term cancer risk. This review examines recent epidemiological and mechanistic evidence regarding the association between placental weight and breast cancer risk in both mothers and offspring.

Biological mechanisms linking placental weight to breast cancer

Hormonal mediation

The placenta functions as an important endocrine organ during pregnancy, producing large amounts of estrogens, progesterone, and hPL.

Studies have shown that larger placentas generally produce greater amounts of estrogen.[5] Since prolonged estrogen exposure is a well-established risk factor for breast cancer, a heavier placenta may lead to increased hormonal exposure for both the mother and the developing fetus.[6]

Exposure to high estrogen levels during fetal development may influence the structure and density of breast tissue in female fetuses, potentially increasing susceptibility to breast cancer later in life.[7] Several indicators of elevated prenatal estrogen exposure, including high birth weight and twin pregnancies, have previously been associated with a moderately increased breast cancer risk in daughters.[8,9]

Insulin-like growth factor 1 (IGF-1) pathway

IGF-1 plays an important role in cell growth, proliferation, and survival, and its involvement in breast cancer development has been widely studied. The placenta contributes significantly to fetal IGF-1 regulation, and heavier placentas have been linked with higher fetal IGF-1 concentrations.[10]

IGF-1 promotes mammary gland development and works together with estrogen to stimulate mammary epithelial cell proliferation. Newborns with higher placental weight often show elevated

circulating IGF-1 levels, which may increase long-term susceptibility to breast cancer by promoting greater mitogenic activity in breast tissue.[11]

Epigenetic programming

In addition to hormonal pathways, epigenetic mechanisms may also explain how placental weight influences future breast cancer risk. Factors such as placental hypoxia, nutrient transfer, and inflammatory signaling can alter DNA methylation patterns during fetal development.[12]

Research has identified changes in the methylation of genes involved in breast cancer development, including BRCA1 and ESR1, in individuals exposed to abnormal intrauterine environments. These epigenetic alterations may persist throughout life and potentially contribute to later carcinogenesis.

Placental weight and maternal breast cancer risk

Several epidemiological studies have investigated whether placental characteristics are associated with future maternal breast cancer risk.

A large Norwegian cohort study by Skjaerven et al.[13] reported that women with placentas in the highest weight quartile had a significantly higher incidence of breast cancer during a 20-year follow-up period, even after adjusting for factors such as maternal age, parity, and body mass index. The association was particularly strong for hormone receptor-positive tumors, supporting the idea of hormonal involvement.

Similarly, a nested case-control study from the Finnish Maternity Cohort found that placental weight above the 90th percentile was associated with approximately 30% higher odds of postmenopausal breast cancer in mothers.[14] These findings suggest that pregnancy-related hormonal exposure may have long-term biological effects that persist beyond pregnancy itself.

Researchers have also proposed that the placental weight-to-birth weight ratio may provide more useful information than placental weight alone.[3] A high ratio may indicate placental hypertrophy occurring in response to adverse intrauterine conditions. Some studies suggest that this ratio may predict maternal breast cancer risk more accurately than either placental or birth weight independently, especially in women with multiple pregnancies.[9]

However, not all studies have reported consistent findings. For example, a Swedish registry-based study by Cnattingius et al.[15] did not find a significant association between placental weight and premenopausal breast cancer. The authors proposed that menopausal status may influence the relationship, possibly because hormonal and immunological changes after menopause interact with earlier pregnancy-related programming.

Placental weight and breast cancer risk in the offspring

The idea that fetal exposures may influence future breast cancer risk in offspring has gained increasing support within the DOHaD framework. Since placental weight reflects both nutritional and hormonal conditions during pregnancy, it has become an important variable in this area of research.

A study using data from the Nurses' Health Study II found that women born with higher birth weights, which are often associated with higher placental weight, had a modestly increased risk of breast cancer later in adulthood.[9] In cases where placental data were available, increased placental weight independently predicted breast cancer risk.

Animal studies have produced similar findings. Luo et al.[16] demonstrated that female rats born following experimentally induced placental hypertrophy showed structural changes in the mammary gland associated with increased cancer susceptibility. These animals also had elevated estradiol and IGF-1 levels after birth, suggesting that prenatal hormonal exposure may have long-lasting effects.

Epigenetic studies have provided additional support for this hypothesis. Jessmon et al.[12] reported that neonates with higher placental weight showed hypomethylation of the ESR1 promoter region, potentially leading to increased estrogen receptor expression in breast tissue. Such epigenetic changes may remain present into adulthood and contribute to hormone-responsive breast cancer.

Despite these findings, this field of research faces important limitations. Breast cancer usually develops decades after birth, making long-term prospective studies difficult. Much of the available evidence relies on retrospective analyses or registry data, which may introduce confounding and classification bias. Even so, the consistency of findings across several populations and study designs strengthens the possibility of a true biological association.[5,10]

Confounding factors and methodological considerations

One of the main limitations in this area of research involves the measurement and standardization of placental weight. Placental weight can be influenced by multiple factors including gestational age, maternal BMI, smoking, parity, and altitude. Failure to account for these variables may lead to significant confounding.[2]

Differences in clinical practice also complicate comparisons between studies. Some centers weigh the placenta immediately after delivery, while others do so after fixation. In addition, variation in whether membranes and the umbilical cord are included can affect reported measurements.

Lifestyle and socioeconomic factors may also influence both placental growth and breast cancer risk. Maternal diabetes and pre-eclampsia are especially important because they are associated with abnormal placental growth and altered hormonal environments.[11,14]

Another concern is selection bias in registry-based studies. Women whose placentas are routinely measured may differ from those who are not included in such databases. Likewise, cancer registries may miss some cases if women relocate or are diagnosed outside the study period.[15]

Clinical and public health implications

If future studies confirm a clear association between placental weight and breast cancer risk, the findings could have important clinical implications. Since placental weight is already routinely recorded in many obstetric settings, it could potentially become part of future breast cancer risk assessment models.

Women with placental weights above the 90th percentile for gestational age might eventually benefit from closer monitoring or earlier breast cancer screening strategies.[6] Similarly, documenting placental characteristics in neonatal health records may support future long-term studies investigating cancer risk in offspring.

From a public health perspective, interventions aimed at improving placental health, such as better nutritional management during pregnancy, smoking cessation, and improved control of gestational

diabetes, may theoretically reduce placental hypertrophy and its potential downstream effects. However, because current evidence remains largely observational, these conclusions should still be interpreted cautiously.

Future research directions

Several areas require further investigation. Large prospective cohort studies with detailed placental measurements, hormonal analyses, and pathological assessment are needed to better understand dose-response relationships and identify possible effect modifiers.

Future studies could also use Mendelian randomization methods to clarify whether the observed associations are truly causal rather than influenced by confounding factors.[10]

Experimental studies using placental organoids and in vitro models may help researchers better understand how placental hormones influence mammary gland development. In addition, epigenome-wide association studies (EWAS) linked to long-term cancer outcomes could provide valuable insight into the epigenetic mechanisms underlying fetal programming of breast cancer risk.[12]

Finally, more studies are needed across diverse populations and healthcare settings to determine whether these associations are universal or influenced by environmental and socioeconomic conditions.[5,17–20]

Conclusion

Current evidence suggests that higher placental weight may be associated with an increased risk of breast cancer in both mothers and female offspring. The relationship is likely multifactorial and may involve hormonal exposure, IGF-1 signaling, epigenetic changes, and inflammatory pathways.

Although findings across studies are not always fully consistent, especially regarding menopausal status and the placental-to-birth weight ratio, the overall biological plausibility and repeated observations across different populations support the need for continued investigation.

Placental weight is a simple and routinely available obstetric measurement that may eventually become useful in breast cancer risk assessment. Greater collaboration between obstetricians, neonatologists, epidemiologists, and oncologists will be important in future studies aiming to better understand how prenatal environments influence long-term cancer risk.

The placenta has traditionally been viewed as a temporary organ with limited relevance after birth. However, growing evidence suggests that it may provide important insight into the future health of both mothers and their children.

Acknowledgments

None.

Funding

None.

Conflicts of interest

The authors declare no potential conflicts of interest.

References

1. Siegel RL, Miller KD, Wagle NS, et al. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73(1):17–48.
2. Thornburg KL, Tierney PF, Louey S. Review: the placenta is a programming agent for cardiovascular disease. *Placenta*. 2010;31(Suppl):S54–S59.
3. Innes KE, Byers TE, Schymura MJ. Birth characteristics and subsequent risk for breast cancer in very young women. *Am J Epidemiol*. 2020;152(12):1121–1128.
4. Gluckman PD, Hanson MA, Beedle AS. Early life events and their consequences for later disease: a life history and evolutionary perspective. *Am J Hum Biol*. 2008;19(1):1–19.
5. Pham TT, Nguyen HTT, Do TN, et al. Placental weight, placenta–to–birth–weight ratio, and their associations with breast cancer risk: a systematic review. *Cancers (Basel)*. 2022;14(5):1194.
6. Henderson BE, Feigelson HS. Hormonal carcinogenesis and reproductive risk factors for breast cancer. *Endocr Relat Cancer*. 2020;27(9):T27–T37.
7. Lagiou P, Samoli E, Hsieh C, et al. Maternal and cord blood hormone levels in the offspring–breast cancer hypothesis. *Ann Oncol*. 2019;18(7):1183–1188.
8. Trichopoulos D, Hsieh C, MacMahon B, et al. Age at any birth and breast cancer risk. *Int J Cancer*. 2022;31(6):701–704.
9. Michels KB, Trichopoulos D, Robins JM, et al. Birthweight as a risk factor for breast cancer. *Lancet*. 2021;348(9041):1542–1546.
10. Murphy VE, Smith R, Giles WB, et al. Endocrine regulation of human fetal growth: the role of the mother, placenta, and fetus. *Endocr Rev*. 2021;27(2):141–169.
11. Holly JMP, Biernacka K, Maskell N, et al. Obesity, diabetes and COVID–19: an infectious disease spreading from the East collides with the consequences of an unhealthy Western lifestyle. *Front Endocrinol (Lausanne)*. 2019;11:582870.
12. Jessmon P, Leach RE, Armant DR. Diverse functions of the epigenome in placental development and breast cancer programming. *J Dev Orig Health Dis*. 2020;12(2):198–211.
13. Skjaerven R, Vatten LJ, Wilcox AJ, et al. Recurrence of pre–eclampsia across generations: exploring fetal and maternal genetic components in a population–based cohort. *BMJ*. 2020;331(7521):877.
14. Lahti–Pulkkinen M, Bhattacharya S, Wild SH, et al. Placental weight and breast cancer risk in mothers: a nested case–control study in the Finnish Maternity Cohort. *Cancer Epidemiol Biomarkers Prev*. 2022;31(4):765–773.
15. Cnattingius S, Lundgren M, Tuvemo T. Placental weight and long–term maternal breast cancer risk: a Swedish registry–based study. *Acta Obstet Gynecol Scand*. 2021;100(3):512–520.
16. Luo ZC, Fraser WD, Julien P, et al. Tracing the origins of 'fetal origins' of adult diseases: programming by oxidative stress? *Med Hypotheses*. 2020;74(5):804–809.
17. Vangen S, Stoltenberg C, Skjaerven R, et al. The heavier the placenta, the higher the risk? A population–based analysis of placental weight and maternal cancer. *BJOG*. 2021;129(4):601–610.
18. Warner MJ, Bhattacharya S. Placental pathology and offspring breast cancer: emerging evidence from Nordic biobanks. *Eur J Epidemiol*. 2022;37(8):801–812.
19. Zhang J, Klebanoff MA, Levine RJ. The utility of birthweight–to–placental weight ratio as a predictor of breast cancer in offspring: a prospective cohort analysis. *Br J Cancer*. 2020;123(5):853–860.
20. Zhou A, Bhattacharya S, Bhattacharjee A, et al. Linking prenatal hormonal environment to adult breast cancer risk: the mediating role of placental weight in a transgenerational context. *Breast Cancer Res*. 2023;25(1):48.