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Research Article

Interrelationship Between Placental Morphology and Thyroid Function in Preeclampsia: A Narrative Review

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ABSTRACT

Background: Preeclampsia is a pregnancy-related disorder, characterized by mild to severe hypertension along with reduced or abnormal function of the placenta. The placenta plays an essential role in the pathogenesis of preeclampsia and increasing changes in maternal thyroid function which may contribute to placental structural and functional abnormalities. Thyroid hormones are crucial for normal placental development, trophoblast differentiation and angiogenesis.

Objective: This narrative review aims to summarize and explore the present literature on the relationship between placental morphological variations and thyroid function modifications in preeclamptic pregnancies.

Methods: A narrative review of published literature showed by electronic databases including PubMed, Scopus, and Google Scholar. This showed existing records on the association between placental morphological variations and thyroid function changes in preeclamptic pregnancies. A narrative approach allow a comprehensive and interpretative discussion of histopathological and experimental findings. The most relevant human and experimental studies, evaluating the placental morphology, histopathological changes and thyroid hormone variations in preeclampsia.

Results: Preeclamptic pregnancies are related with placental morphological changes, including reduced placental weight, villous hypoplasia, increased syncytial knots, fibrinoid necrosis, and impaired vascularization. Simultaneously, thyroid function changes, elevated thyroid-stimulating hormone levels and reduced free thyroxine are commonly stated in women with preeclampsia. Many studies suggests that thyroid hormone imbalance may impair abnormal placentation through reduced trophoblast invasion, changed angiogenic signaling, oxidative stress and deregulation of placental deiodinase activity. The thyroid hormone signaling promotes placentation, while anomalous thyroid hormone signaling leads to malplacentation and causing pregnancy associated complications, such as preeclampsia. In this review, we summarize current knowledge of placental dysfunction with association of thyroid hormone imbalance in preeclamptic pregnant women. Future research should focus on advancing placental studies in populations affected by thyroid hormone imbalance.

Conclusion: Understanding how thyroid hormones interact with placental structure can

provide insight into disease development and emphasizes the value of early thyroid function testing in preeclampsia.There is limited research on placenta particular to preeclamptic women with association of thyroid dysfunction. Thyroid hormone imbalance interrupt normal placental development, causing structural and functional abnormalities. Additional research is needed to prevent adverse maternal and fetal outcomes in pre-eclamptic pregnancies.

Key words: Placenta, Thyroid hormone, Preeclamptic women, Prevention.

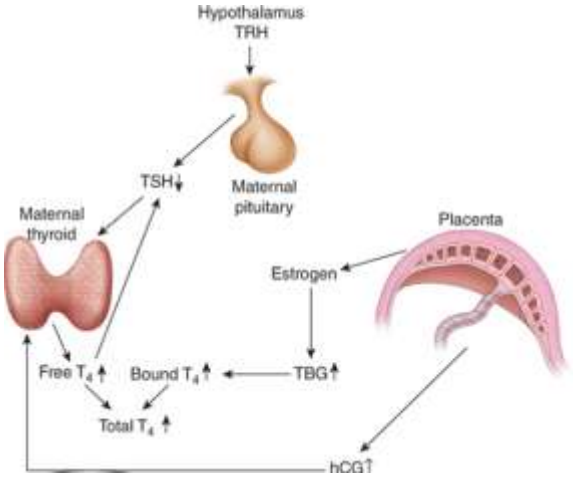
INTRODUCTION

Overview of Placentation

Placentation is the process in which the placenta develops during pregnancy and it provides the exchange of nutrient, gas and waste products between mother and fetus. It starts after implantation of the blastocyst and involves several steps. The outer layer of the blastocyst, the trophoblast, which is distinguish into a proliferative inner layer, cytotrophoblast and a multinucleated outer layer, syncytiotrophoblast that inhabit in the maternal endometrium. During implantation, the blastocyst implant into the endometrium with the syncytiotrophoblast digesting maternal tissue to permit attachment (1). This is precede by the formation of chorionic villi, which development from primary villi, consisting of a cytotrophoblast core covered by syncytiotrophoblast to secondary villi, where mesoderm invades the core and finally to tertiary villi, which develop fetal capillaries to allow maternal-fetal exchange. As gestation advances, the placenta grow into a maternal side (decidua basalis) and a fetal side (chorionic plate). Thus, secreting hormones such as hCG, progesterone, estrogens, PGH, relaxin, HPL. These hormone regulates the immune tolerance, nutrient transfer and waste removal (2).

Transportation of Thyroid hormones across the Placenta

The placenta plays a critical role in regulating maternal thyroid hormone transfer to the fetus, which is necessary for the neurological growth of fetus. Maternal T4 and T3 cross the placenta, where deiodinase enzymes control hormone accessibility: D2 converts T4 to active T3, while D3 inactivates excess hormones to protect the fetus (3). Maternal thyroid hormone production is controlled by the hypothalamic–pituitary–thyroid (HPT) axis, while placental hCG helps stimulate the mother's thyroid and pregnancy-related estrogen increases thyroid-binding globulin levels. These mechanisms assure adequate thyroid hormone availability for normal placental function and fetal development (4).



Puthiyachirakal, AlNatsheh, T. et al. Overview of thyroid disorders in pregnancy. matern health, neonatol and perinatol 11, 9 (2025) (5).

Metabolism of Thyroid Hormones in the Placenta

The placenta modulate fetal thyroid hormone through metabolism and deiodination. The D2 activates T4 to T3, increasing local hormone accessibility and the D3 inactivates T4 and T3 to defend the fetus. Thyroid hormone are transported into placental cells via MCT8 (Monocarboxylate Transporter 8), MCT10 (Monocarboxylate Transporter 10), LATs (L-type Amino Acid Transporters) and OATPs (Organic Anion Transporting Polypeptides) before deiodination (6). These are transport proteins for the placenta that help the thyroid hormones (T3 and T4) and another molecules into placental cells to regulate fetal thyroid hormone. This thyroid signaling also helps in trophoblast function, angiogenesis and vascular remodeling. Abnormal metabolism, such as low D2 or high D3 activity, can lead to fetal hypothyroidism, diminished placental function and other complications like preeclampsia, growth restriction, and preterm birth (7).

Regulation of Placentation by Thyroid Hormones

Thyroid hormones play a key role in the development of placenta and stimulate trophoblast proliferation, formation of the placental villous structure, extravillous trophoblast invasion and spiral artery remodeling, which are necessary for converting maternal spiral arteries into low-resistance vessels and provide sufficient placental perfusion (8). In addition, these hormones support the maternal-fetal nutrient and oxygen exchange and it also regulates the placental metabolism, including energy regulation, oxidative stress response and enzyme activity. Dysfunction of thyroid hormones during pregnancy can damage these processes, lead to abnormal development of placenta which may contribute to complications such as preeclampsia, intrauterine growth restriction and miscarriage (9).

Definition and Pathology of Preeclampsia

Preeclampsia is a multisystem hypertensive disorder of pregnancy, occurring after 20 weeks of gestation, and remains a leading cause of maternal and perinatal morbidity and mortality worldwide (10). In spite of broad research, the detailed etiology of preeclampsia is not fully understood. Though, abnormal placentation and placental dysfunction are usually recognized as central to its pathogenesis. The placenta plays a serious role in maintaining maternal fetal homeostasis and structural or functional disorders with this organ can considerably influence pregnancy outcomes (11). The development of normal placenta depends on adequate trophoblast invasion, proper transformation of spiral arteries and well-regulated angiogenesis. In preeclampsia, these processes are diminished, causing in reduced uteroplacental perfusion, placental hypoxia, oxidative stress, and inflammation. These pathological conditions manifest as distinctive placental morphological variations and reduced villous vascularization. Such structural abnormalities compromises exchange of placental capacity and can cause fetal growth restriction (12).

Thyroid hormones play a key role in normal pregnancy by regulating maternal metabolism, fetal growth and placental development. The placenta not only transfer the thyroid hormones from mother to fetus but also actively controls

their local accessibility by the expression of thyroid hormone transporters and deiodinase enzymes(13). The change in maternal thyroid function, particularly hypothyroidism and subclinical hypothyroidism have been progressively linked with hypertensive disorders of pregnancy, including preeclampsia (14). Many studies have stated elevated thyroid-stimulating hormone levels and decreased circulating thyroxine concentrations in preeclamptic women, proposing a strong link between thyroid dysfunction and disease severity. Developing suggestion shows that thyroid hormone imbalance may effect placental structure and function by harming trophoblast proliferation and invasion, varying angiogenic signaling pathways and growing oxidative stress within placental tissue(14).

On the other hand, placental hypoxia and dysfunction characteristic of preeclampsia may interrupt local thyroid hormone metabolism, producing a bidirectional association between thyroid function and placental pathology. Therefore, this narrative review aims to summarize and assess current evidence on placental morphological and thyroid function changes in preeclampsia (15). A healthier understanding of this association may deliver insight into the pathophysiology of preeclampsia and highlight the possible role of thyroid function assessment in improving maternal and fetal outcomes. Hence, disruption in thyroid functions may evident as changed placental structure, which may further causing the development or severity of PE (16). The abnormalities in placental structure are seen in pre-eclamptic pregnancies, causing vascular insufficiency and inadequate trophoblast invasion. In PE, the placenta presents with reduced size and weight, infarctions, fibrinoid necrosis, and perivillous fibrin deposition that compromised maternal blood flow. Microscopically, these placentas exhibit an increased number of syncytial knots, poorly branched villi, advance calcification, intervillous thrombosis and spiral artery atherosis, all indicative of under chronic hypoxic stress and effect on maternal–fetal exchange (17). Therefore, even elusive alterations in thyroid hormone levels may play a role in boost or worsening the placental morphological abnormalities mostly seen in pre-eclampsia.

Risk factors for Preeclampsia :

Include first pregnancy, a previous history of preeclampsia a family history of chronic hypertension, thyroid disorders, diabetes mellitus, kidney disease and the other risk factors include obesity, advanced maternal age (35 years or older), multiple pregnancies such as twins, the use of reproductive techniques like IVF and poor placentation or abnormal placental development. These factors increase the risk by affecting blood vessels, immune response or placental function (18)..

Thyroid Function Alterations in Pre-eclampsia

Alterations in maternal thyroid function are progressively recognized as contributive factors in pre-eclampsia. Women with PE often present with elevated TSH, or reduced free T4 levels, even when values fall within the borderline-normal range. These changes may indicate the body's response to enhance metabolic demand and systemic inflammation characteristic of PE (19).

Dysfunctional placenta may also decrease the conversion of thyroxine (T4) to the active form triiodothyronine (T3), causing maternal–fetal thyroid hormone imbalance. In addition, the anti-angiogenic factors can also interfere and lead to decreased hormone synthesis. As thyroid hormones regulates the metabolic rate and important for fetal neurodevelopment, even mild

dysfunction may have physiological worst consequences in preeclamptic pregnancies (20)..

Interrelation between placental damage and thyroid dysregulation

This relate to how damage or dysfunction in the placenta can be associated with disturbances in normal thyroid hormone regulation. Placental abnormalities and thyroid dysfunction in PE are dependent processes that may exaggerate each other. A structurally compromised placenta may limit the transfer of iodine and thyroid hormones between mother and fetus, interupting endocrine balance. At the same time, deficient thyroid hormones can damage trophoblast proliferation, placental angiogenesis, and spiral artery remodeling, all of which are dangerous for healthy placental development. Thus, thyroid hormone dysregulation may degenerate placental insufficiency, though placental hypoxia and oxidative stress may interrupt thyroid hormone functions(19).

Biological mechanisms linking thyroid hormone activity to placental structure

Various molecular and physiological pathways connect thyroid hormone disturbances with the placental morphological changes characteristic of PE (21):

a. Dysfunctional Trophoblast Invasion

Thyroid hormones (T3 and T4) encourage cytotrophoblast differentiation and extravillous trophoblast invasion. Decreased levels of thyroid hormones may lead to shallow invasion of spiral arteries, resulting in deficient maternal blood flow and the structural imperfection commonly observed in PE placentas (21).

b. Oxidative Stress and Hypoxia

This play a key role in placental dysfunction, particularly in preeclampsia. Together, hypoxia and oxidative stress initiate inflammation and the release of noxious factors into the maternal circulation. This contribute to endothelial dysfunction, high blood pressure and placental injury, deteriorating both maternal and fetal outcomes. Both thyroid dysfunction and placental underperfusion increase oxidative stress. Hypoxia-induced oxidative damage and cause villous aging, fibrinoid necrosis and syncytial knot formation (22).

c. Altered Vascular Remodeling

This refers to abnormal changes in the blood vessels of the placenta, which is a characteristic feature of preeclampsia. Usually in pregnancy, maternal spiral arteries go through remodeling to transform wider and low-resistance vessels. This allows a sufficient blood supply to the placenta.
In preeclampsia, this remodeling process is abnormal. The arteries remains narrow and immobile, leading to decreased blood flow. This can cause placental ischemia, oxidative stress and injury to placental tissues. Thyroid hormone influences vascular smooth muscle relaxation and endothelial function. The hormonal imbalance can damage vascular remodeling of maternal spiral arteries, promoting lesions such as atherosis and thrombosis seen in PE (23).

d. Disrupted Maternal–Fetal Hormone Transport

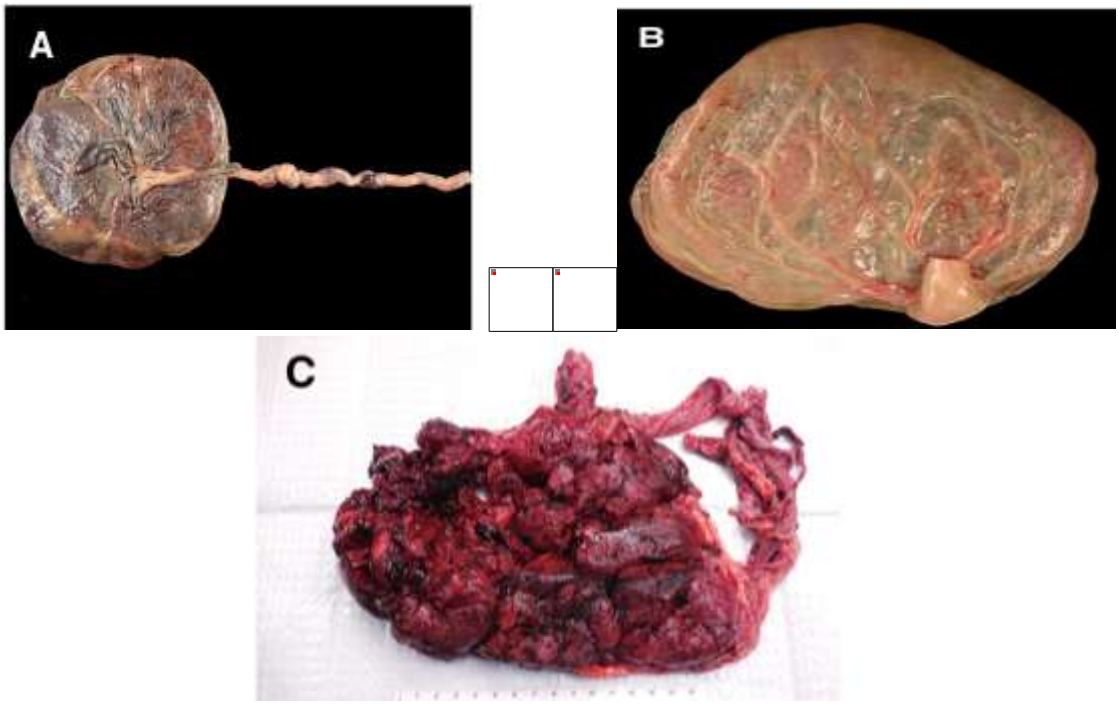
Placental dysfunction may extent the transport of thyroid hormones and iodine, reducing hormone availability for both mother and fetus. This further aggravate thyroid dysregulation, creating a feedback loop that worsens placental pathology (23).

Macroscopic and Microscopic Placental Changes Observed in Preeclamptic Pregnancies

In preeclamptic pregnancies, the changes occurs

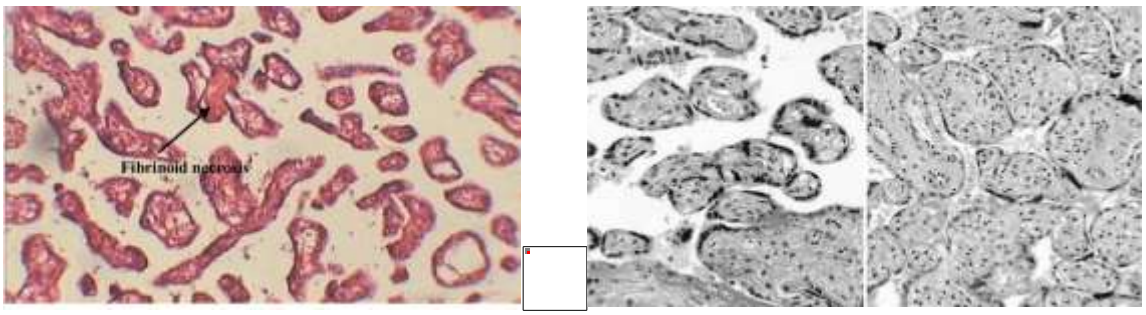
in placenta that can be seen both with the macroscopic and under the microscope:

Macroscopic changes occurs as a smaller-than-normal placenta, areas of infarction (localized tissue death), increased firmness and an irregular surface. The gross examination of the placenta shows **A.** discolored membranes with a tight knot of the umbilical cord. **B.** The membranes are discolored due to chorioamnionitis and **C.** The fragmented placenta. These findings indicate decreased blood flow and dysfunctional placental development (24).



Criteria for placental examination for obstetrical and neonatal providers Roberts, Drucilla J. et al. American Journal of Obstetrics & Gynecology, Volume 228, Issue 5, 497 - 508.

Microscopic changes occurs as abnormal development of placental blood vessels, diminished branching of villi, thickening of vessel walls, fibrinoid necrosis, syncytial knot and shows signs of ischemia. Conjointly, these occurrence indicate poor placental perfusion and poor exchange of oxygen and nutrients between mother and fetus (24).



Fibrinoid Necrosis **Syncytial Knot**

Loukeris K, Baergen RN. Syncytial knots as a reflection of placental maturity: Pediatric and developmental pathology. 2010 Jul;13(4):305-9.

Search strategy and article selection criteria

A comprehensive literature was studied to explore the relationship between thyroid function and placental structure in the context of preeclampsia. Electronic databases including PubMed/MEDLINE, Scopus, Embase, Web of Science, and the Cochrane Library were searched from January 1, 2002 to December, 2025.

Principal Points

·Thyroid hormones play a chief role in the development of placenta, promotes trophoblast proliferation, differentiation and invasion.

· Abnormal maternal thyroid function can change TSH, T3, and T4 levels and are associated with impaired placentation.

·Thyroid hormone dysregulation can lead to abnormal spiral artery remodeling, resulting in decreased placental perfusion and structural abnormalities.

· The placenta controls how much thyroid hormone reaches the fetus via special transport proteins and enzymes (D2 and D3), which maintain hormone levels and normal placental structure.

· Altered placental structure, such as reduced villous branching and increased infarction, may affect maternal thyroid hormone metabolism and circulating hormone levels.

· The interaction between thyroid dysfunction and placental abnormalities may develop pregnancy complications such as preeclampsia and intrauterine growth restriction.

· Early analysis of maternal thyroid function tests may help in identifying pregnancies at risk for placental pathology and adverse outcomes.

Conclusions

Many studies demonstrate interrelationship between placental morphology and thyroid dysfunction in preeclampsia. Placental abnormalities compromised hormone production and transport. Concurrently, thyroid dysfunction changed placental thyroid hormone transport and may worsen placental insufficiency. This bidirectional interaction mark the placenta's central role in linking vascular, endocrine and inflammatory pathways in the pathogenesis of preeclampsia.

Future Strategies and Directions

Integrated Clinical Screening

Regular assessment of thyroid function, especially in women at high risk for preeclampsia, should be considered placental and Doppler evaluations. Early determination of harmful thyroid abnormalities may help predict disease advancement.

Placental Biomarker Research

Further studies are required to see placental biomarkers related to thyroid hormone metabolism (e.g., thyroid hormone receptors) that may contribute to early indicators of placental dysfunction in preeclampsia.

Molecular and Histopathological Correlation Studies

Large-scale studies correlating placental histomorphology with maternal and fetal thyroid hormone levels, can elucidate mechanisms and disease intensity associations.

Therapeutic Interventions

Investigating maternal thyroid function during early pregnancy can improve placental development and decrease the relative incidence or severity of preeclampsia is an essential future research direction.

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