

Riporto per gli studenti un recente articolo sulla recente relazione tra le malattie autoimmune e la gravidanza ad integrazione degli altri articoli sempre sulle Malattie autoimmune.

Autoimmune Thyroid Disease and Pregnancy

Author: Dotun A Ogunyemi, MD, Associate Professor of Obstetrics and Gynecology, David Geffen School of Medicine at UCLA; Residency Program Director, Clerkship Director, Department of Obstetrics and Gynecology, Cedars Sinai Medical Center

Updated: Apr 23, 2010

Background

Thyroid disorders are the second most common endocrinologic disorders found in pregnancy. Overt hypothyroidism is estimated to occur in 0.3-0.5% of pregnancies. Subclinical hypothyroidism appears to occur in 2-3%, and hyperthyroidism is present in 0.1-0.4%.

Autoimmune thyroid dysfunctions remain a common cause of both hyperthyroidism and hypothyroidism in pregnant women. Graves disease accounts for more than 85% of all cases of hyperthyroid, whereas Hashimoto thyroiditis is the most common cause of hypothyroidism.

Postpartum thyroiditis (PPT) reportedly affects 4-10% of women. PPT is an autoimmune thyroid disease that occurs during the first year after delivery. Women with PPT present with transient thyrotoxicosis, hypothyroidism, or transient thyrotoxicosis followed by hypothyroidism. This presentation may be unrecognized, but is important because it predisposes the woman to develop permanent hypothyroidism.

Of interest, symptoms of autoimmune thyroid diseases tend to improve during pregnancy. A postpartum exacerbation is not uncommon and perhaps occurs because of an alteration in the maternal immune system during pregnancy. The improvement in thyroid autoimmune diseases is thought to be due to the altered immune status in pregnancy.

Pathophysiology

The defect that predisposes an individual to develop autoimmune thyroid disease is still unknown. Proposed mechanisms include a tissue-specific defect in suppressor T-cell activity, a genetically programmed presentation of a thyroid-specific antigen, and an idiootype/anti-idiootype reaction. Regardless of the cause, the common outcome is the production of 1 or more types of autoantibodies.

Graves disease

Adams and Purves described the concept of Graves disease as an autoimmune dysfunction of the thyroid gland. These investigators noted that the sera of patients with Graves disease contained a factor that stimulated the murine thyroid gland. This factor had a longer duration of action than that of thyrotropin (ie, thyroid-stimulating hormone [TSH]), the long-acting thyroid stimulator.

Further studies revealed that these long-acting thyroid stimulators are autoantibodies directed against the TSH receptor. The activating versions of the TSH receptor are the thyroid-stimulating autoantibodies, which activate adenylate cyclase and which stimulate thyroid function.

In terms of histologic features, the thyroid glands of patients with Graves disease show follicular hypertrophy and hyperplasia.

Hashimoto thyroiditis

Hashimoto thyroiditis is also known as goitrous chronic thyroiditis. Almost all patients with this disease have positive test results for the thyroid peroxidase antibody (anti-TPO), an autoantibody against thyroid peroxidase enzyme. Of these patients, 50-70% also have positive results for antithyroglobulin antibodies.

Classic histologic findings of Hashimoto thyroiditis are extensive lymphocytic infiltration, follicular rupture, eosinophilia, various degrees of hyperplasia, and fibrosis.

Atrophic chronic thyroiditis

Atrophic chronic thyroiditis is a rare autoimmune cause of hypothyroidism. This condition is characterized by the presence of blocking autoantibodies to the TSH receptors.

Postpartum thyroiditis

PPT is a variant of chronic autoimmune thyroiditis (Hashimoto thyroiditis). PTT is characterized by the presence of antimicrosomal antibodies. Histologic examination of PTT-affected thyroid glands affected reveals destructive lymphocytic thyroiditis.

Frequency

United States

Hyperthyroidism affects 0.1-0.4% of pregnancies. Graves disease accounts for 85% of these cases. Hypothyroidism affects up to 2.2% of pregnant women and Hashimoto thyroiditis is the most common cause. Atrophic thyroiditis is less common. Postpartum thyroiditis has a prevalence ranging from 3.3-8.8% in the United States.

International

The reported range for the frequency of PPT is wide. In Thailand, as few as 2 in 100 postpartum women are affected. By comparison, some Canadian studies revealed a frequency of 2 per 10 postpartum women. These differences may be due to variations in diagnostic criteria, in genetic factors, and in iodine consumption.

Mortality/Morbidity

Fetal and maternal outcomes improve when thyroid function returns to normal.

Hyperthyroidism

Uncontrolled hyperthyroidism, especially in the second half of pregnancy, can lead to numerous complications. Maternal complications include miscarriage, infection, preeclampsia, preterm delivery, congestive heart failure (CHF), thyroid storm, and placental abruption. Fetal and neonatal complications include prematurity, small size for gestational age, intrauterine fetal death, and fetal or neonatal goiter and/or thyrotoxicosis. Overtreatment may cause iatrogenic fetal hypothyroidism.

Hypothyroidism

Maternal complications of untreated hypothyroidism include microcytic anemia, preeclampsia, placental abruption, postpartum hemorrhage, cardiac dysfunction, and miscarriage. Fetal or neonatal complications include prematurity, low birth weight, congenital anomalies, stillbirth, and poor neuropsychological development.

In particular, overt maternal hypothyroidism is associated with neonatal neurologic developmental delay because of the transplacental transfer of thyroid hormone in early pregnancy is inadequate. This process is required for brain development. The fetal thyroid does not begin to concentrate iodine until 10-12 weeks of gestation. Therefore, before this time, the mother must provide for all of the fetus' thyroxine (T4) requirements.

Approximately 10-15% of the population has thyroid antibodies. These antibodies have been linked to an increased risk of spontaneous abortion.

Subclinical hypothyroidism also has been associated with spontaneous abortion and with preterm labor.

Postpartum thyroiditis

Complications associated with PPT are maternal, and depression is common. Permanent hypothyroidism occurs in as many as 30% of women. These patients are also at high risk for recurrent PPT with subsequent pregnancies.

Sex

Autoimmune thyroid diseases occur more often in women than in men. The female-to-male ratio is 5-10:1.

Age

Autoimmune thyroid dysfunction most often affects women of reproductive age.

Clinical

History

Symptoms of hyperthyroidism can be easily confused with symptoms of the hypermetabolic state of pregnancy. Mild hypothyroid symptoms can be difficult to distinguish from the common aches and pains of pregnancy. Obtaining a careful patient history is essential in the evaluation of women thought to have thyroid dysfunction.

Hyperthyroidism

- Patients with hyperthyroidism usually report loss of concentration, nervousness, and emotional lability.
- Tremor, heat intolerance, excessive sweating, palpitations, and hyperdefecation are also common findings.
- Patients may report having difficulty with climbing stairs; this is a sign of proximal muscle weakness.
- Some patients may report that their neck is getting bigger than it was before. This change is caused by the enlarged thyroid gland.

Hypothyroidism

- Untreated patients with moderate-to-severe hypothyroidism have impaired fertility. As a result, women with this disease are rarely pregnant at the time of presentation.
- Symptoms of mild hypothyroidism can mimic those of normal pregnancy, making diagnosis difficult.
- Lethargy, weight increase, and constipation are commonly reported.
- Patients frequently report having cold intolerance, stiffness, muscle cramping, carpal tunnel syndrome, dry hair and skin, and a deepened voice.

Postpartum thyroiditis

- PPT has 3 phases:
 1. Hyperthyroid phase, when thyroid hormones are being released because of thyroid destruction
 2. Hypothyroid phase
 3. Resolution, or euthyroid, phase
- The most common time for women present with PPT is 1-8 months after delivery, with a peak incidence at 6 months. This timing is important because the process may overlap with the next pregnancy in women who have short pregnancy intervals.
- Depending on the stage of disease at the time of presentation, patients may have symptoms of hyperthyroid or hypothyroid, as outlined above.

Subclinical hypothyroidism

- Subclinical hypothyroidism affects 2-3% of women in pregnancy.
- The symptoms of subclinical hypothyroidism are vague and nonspecific.
- The diagnosis is based on a normal level of free thyroxine (FT4) and an elevated TSH level.

Physical

Hyperthyroidism

- General appearance: In general, patients with hyperthyroidism are restless, anxious, and fidgety.
- Skin and hair: The patient's skin is warm and moist, with a velvety texture, and their hair is fine and silky.
- Eyes
 - The eyes usually have a characteristic stare, with a widened palpebral fissure.
 - Lid lag and failure to wrinkle the brow during the upward gaze are common findings.
 - With careful observation, infrequent blinking is noted.
 - With the infiltrating ophthalmopathy of Graves' disease, potential findings include proptosis, ophthalmoplegia, chemosis, conjunctivitis, periorbital swelling, corneal ulceration, optic neuritis, and optic dystrophy.
- Thyroid
 - A goiter is present in almost every pregnant patient with Graves' disease.
 - The gland is diffusely enlarged, usually 2-4 times normal.
 - The gland can be soft or firm, and it is seldom tender to palpation.
 - A thrill or bruit may be present.
 - Thoroughly examine the thyroid gland for nodules. The presence of a nodule requires further workup during pregnancy to rule out malignancy.
- Heart
 - Findings on cardiac examination include a wide pulse pressure due to increased systolic pressure and decreased diastolic pressure.
 - Sinus tachycardia is common. A resting tachycardia greater than 100 bpm that does not change with Valsalva is helpful in distinguishing hyperthyroid tachycardia from that of pregnancy.
 - Atrial arrhythmias can also be found on examination. These usually occur in the form of atrial fibrillation.
 - Other findings are systolic murmurs, an increased intensity of the apical first sound, cardiac enlargement, and cardiac failure.
- Nails
 - Separation of the nail from the distal nail bed, known as onycholysis or Plummer nail, can often be found when the extremities are examined. The ring fingers are most commonly affected.
 - Fine tremor of the fingers and hyperreflexia can also be noted.

Fetal thyroid dysfunction

- Suggestive findings
 - Fetal tachycardia (fetal heart rate >160 bpm)
 - Intrauterine growth restriction
 - Fetal goiter
 - Hydrops
- Causes
 - The risk of fetal or neonatal thyrotoxicosis is related to the mother's level of thyroid receptor-stimulating antibodies because the antibodies freely cross the placenta.

- o Fetal or neonatal hypothyroidism may also be due to maternal use of antithyroid drugs (ATDs), as these cross the placenta.
- Diagnosis and screening
 - o Fetal diagnosis requires umbilical cord sampling to differentiate hyperthyroidism from hypothyroidism.
 - o In women with a past or current history of autoimmune thyroid disease, thyroid antibody values should be checked at the end of the first pregnancy. For those with positive results for thyroid receptor–stimulating antibodies or those taking ATDs, fetal ultrasonography should be performed at least monthly after 20 weeks of gestation.
- Treatment
 - o Fetal thyroid dysfunction is treated with adjustment of maternal ATD therapy.
 - o Fetal hypothyroidism may require intra-amniotic administration of T4.

Hypothyroidism

- Motor function and cognition: Patients with hypothyroidism appear to have slowing of speech and movement. They can also be forgetful and exhibit difficulty with concentration.
- Skin: The skin is usually dry, pale, and yellowish.
- Hair: Hair is thin, brittle, and sparse.
- Head, eyes, ears, nose, and throat
 - o Auditory acuity may be decreased.
 - o Eye examination may reveal periorbital puffiness.
 - o A large tongue and an expressionless face can be observed in patients with severe disease.
- Thyroid gland
 - o A goiter associated with Hashimoto thyroiditis is firm, diffusely enlarged, and usually painless to palpation.
 - o In patients with atrophic chronic thyroiditis, the thyroid gland may be normal or not palpable.
- Heart
 - o A low-normal heart rate is common.
 - o The heart can be enlarged if it is dilated.
 - o Pericardial effusion is present in severe cases.
- GI tract
 - o Bowel sounds may be decreased or absent.
 - o Paralytic ileus has been reported in severe cases of hypothyroidism.
- Extremities: Examination of the extremities may reveal nonpitting edema and hyporeflexia, with prolongation of the relaxation phase of the reflex response.
- Fetus: Fetal examination usually reveals normal findings in mild cases.

Postpartum thyroiditis

- Presenting findings: Patients with PPT can present with symptoms of hyperthyroidism or hypothyroidism, depending on the stage of disease.
- Phases of disease: As many as one third of women with PPT present with hyperthyroidism at 1-4 months after birth. This period is followed by a hypothyroid phase lasting as long as 2 months. Recovery then ensues.

Causes

The defect that predisposes an individual to develop autoimmune thyroid disease is still unknown. Proposed mechanisms include a tissue-specific defect in suppressor T-cell activity, a genetically programmed presentation of a thyroid-specific antigen, and an idiotypic/anti-idiotypic reaction. Regardless of the cause, the common outcome is the production of 1 or more types of autoantibodies.

