

MANAGEMENT OF THYROID DISORDERS IN PREGNANCY

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PJR Jan - Mar 2008; 18(1): 9-11

Thyroid disease is present in 2-5 percent of all women and 1-2 percent of women in the reproductive age group. Thyroid disorders are the second most common endocrinological 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%.¹

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 hyperthyroidism, whereas Hashimoto thyroiditis is the most common cause of hypothyroidism. Postpartum thyroiditis (PPT) reportedly affects 4-10% of women is again an autoimmune disease.¹¹

Thyroid Function and Morphology in Pregnancy

A normal pregnancy results in a number of important physiological and hormonal changes that alter thyroid function. These changes mean that laboratory tests of thyroid function must be interpreted with caution during pregnancy. Thyroid function tests change during pregnancy due to the influence of two main hormones: human chorionic gonadotropin (hCG), the hormone that is measured in the pregnancy test and estrogen, the main female hormone. hCG can weakly turn on the thyroid and the high circulating hCG levels in the first trimester may result in a slightly low TSH. When this occurs, the TSH will be slightly decreased in the first trimester and then return to normal throughout the duration of pregnancy. Estrogen increases the amount of thyroid hormone binding proteins in the serum which increases the total thyroid hormone levels in the blood since >99% of the thyroid hormones in the blood are bound to these proteins. However,

measurements of "Free" hormone (that not bound to protein, representing the active form of the hormone) usually remain normal. The thyroid is functioning normally if the TSH, Free T4 and Free T3 are all normal throughout pregnancy.²

The thyroid gland can increase in size during pregnancy. However, pregnancy-associated goiters occur much more frequently in iodine-deficient areas of the world. It is relatively uncommon in the United States, which is thought to be relatively iodine-sufficient. If very sensitive imaging techniques (ultrasound) are used, it is possible to detect an increase in thyroid volume in some women. This is usually only a 10-15% increase in size and is not typically apparent on physical examination by the physician. However, sometimes a significant goiter may develop and prompt the doctor to measure tests of thyroid function.⁶

Hypothyroidism in Pregnancy

Approximately, 2.5% of women will have a slightly elevated TSH of greater than 6 and 0.4% will have a TSH greater than 10 during pregnancy.⁴ Overall, the most common cause of hypothyroidism is the autoimmune disorder known as Hashimoto's thyroiditis. Other common causes are inadequate treatment of a woman already known to have hypothyroidism from a variety of causes, or over-treatment of a hyperthyroid woman with anti-thyroid medications.

If untreated, or inadequately treated, hypothyroidism may manifest with maternal anemia, myopathy, congestive heart failure, pre-eclampsia, placental abnormalities, low birth weight infants, and postpartum hemorrhage (PPH). These complications are more likely to occur in women with severe hypothyroidism. Most women with mild hypothyroidism may have no symptoms or attribute symptoms they may have as due to the pregnancy.

Untreated severe hypothyroidism in the mother can lead to impaired brain development in the baby. This is mainly seen when the maternal hypothyroidism is due to iodine deficiency, which also affects the baby.

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Recent research has suggested increased risk of lower IQ of children of women with hypothyroidism, even with euthyroid fetus as maternal thyroid hormone needed for neuronal development until 12-13 weeks.⁵ The treatment of hypothyroidism in a pregnant woman is the same as for a man or non-pregnant woman, namely, adequate replacement of thyroid hormone in the form of synthetic levothyroxine. It is important to note that levothyroxine requirements frequently increase during pregnancy, often times by 25-50%. Occasionally, the levothyroxine dose may double. Ideally, hypothyroid women should have their levothyroxine dose optimized prior to becoming pregnant. Women with known hypothyroidism should have their thyroid function tested as soon as pregnancy is detected and their dose adjusted by their physician as needed to maintain a TSH in the normal range. Thyroid function tests should be checked approximately every 6-8 weeks during pregnancy to ensure that the woman has normal thyroid function throughout pregnancy. If a change in levothyroxine dose is required, thyroid tests should be measured 4 weeks later. As soon as delivery of the child occurs, the woman may go back to her usual pre-pregnancy dose of levothyroxine. It is also important to recognize that prenatal vitamins contain iron that can impair the absorption of thyroid hormone from the gastrointestinal tract. Consequently, levothyroxine and prenatal vitamins should not be taken at the same time and should be separated by at least 2-3 hrs.⁸

Hyperthyroidism in Pregnancy

Overall, the most common cause (80-85%) of maternal hyperthyroidism during pregnancy is Graves' disease and occurs in 0.2% pregnant patients.¹² In addition to other usual causes of hyperthyroidism, very high levels of hCG, seen in severe forms of morning sickness (hyperemesis gravidarum), may cause transient hyperthyroidism. The diagnosis of hyperthyroidism can be somewhat difficult during pregnancy, as radionuclide thyroid scanning is contraindicated during pregnancy due to the small amount of radioactivity, which can be concentrated by the baby's thyroid. Consequently, diagnosis is based on a careful history, physical exam and laboratory testing.

Graves' disease may present initially during the first trimester or may be exacerbated during this time in a woman known to have the disorder.³ In addition to the classic symptoms associated with hyperthyroidism,

inadequately treated maternal hyperthyroidism can result in premature labor, pre-eclampsia or higher risk of developing very severe hyperthyroidism known as thyroid storm. Graves' disease often improves during the third trimester of pregnancy and may worsen during the post partum period.⁹ The risks to the baby from Graves' disease are due to one of three possible mechanisms: 1) uncontrolled maternal hyperthyroidism: has been associated with fetal tachycardia, low birth weight, prematurity, stillbirths and possibly congenital malformations. This is another reason why it is important to treat hyperthyroidism in the mother; 2) extremely high levels of thyroid stimulating immunoglobulin (TSI) which do cross the placenta and can interact with the baby's thyroid resulting in fetal or neonatal hyperthyroidism; 3) anti-thyroid drug (ATD) like methimazole, carbimazole or propylthiouracil (PTU) can cross the placenta and can potentially impair the baby's thyroid function and cause fetal goiter. Mild hyperthyroidism (slightly elevated thyroid hormone levels, minimal symptoms) often is monitored closely without therapy as long as both the mother and the baby are doing well. When hyperthyroidism is severe enough to require therapy, anti-thyroid medications (carbimazole, methimazole and propylthiouracil) are the treatment of choice. A controversial association exists between methimazole and fetal scalp defects, aplastic cutis, and choanal and/or esophageal atresia.¹³ Therefore, PTU tends to be the first choice in this class of drugs. The goal of therapy is to keep the mother's free T4 and free T3 levels in the high-normal range on the lowest dose of antithyroid medication. Targeting this range of free hormone levels will minimize the risk to the baby of developing hypothyroidism or goiter. Maternal hypothyroidism should be avoided. Therapy should be closely monitored during pregnancy. This is typically done by following thyroid function tests (TSH and thyroid hormone levels) monthly. In patients who cannot be adequately treated with anti-thyroid medications (i.e. those who develop an allergic reaction to the drugs), surgery is an acceptable alternative. Surgical removal of the thyroid gland is only very rarely recommended in the pregnant woman due to the risks of both surgery and anesthesia to the mother and the baby. Second trimester is considered as the safest period for surgical option.¹⁰ Radioiodine is contraindicated to treat hyperthyroidism during pregnancy since it readily crosses the placenta and can destroy the fetal thyroid gland resulting in permanent hypothyroidism.

Beta-blockers can be used to control palpitations and tremor due to hyperthyroidism. They should be used sparingly due to reports of impaired fetal growth associated with long term use of these medications.¹³ Typically, these drugs are only required until the hyperthyroidism is controlled with anti-thyroid medications. Graves' disease typically worsens in the postpartum period, usually in the first 3 months after delivery and requires higher doses of anti-thyroid medications.⁷

Post Partum Thyroiditis (PPT)

Postpartum thyroiditis has a prevalence ranging from 3.3-8.8% in the United States.⁷ This is a variant of chronic autoimmune thyroiditis (Hashimoto thyroiditis). PTT is characterized by the presence of anti-microsomal antibodies, also called anti-thyroid peroxidase antibodies (anti TPO). Complications associated with PPT are maternal, and depression is common. These patients are also at high risk for recurrent PPT with subsequent pregnancies. The most common time for women present with PPT is 1-8 months after delivery, with a peak incidence at 6 months.¹¹ Typically, it consists of a temporary period of hyperthyroidism lasting from six weeks to three months postpartum, followed by hypothyroidism between three and nine months after delivery followed by complete recovery in majority of patients. However, permanent hypothyroidism occurs in as many as 30% of women. Management depends upon the phase of disease like beta blocker most commonly or short course of antithyroid medication less commonly for thyrotoxic female and replacement doses of levothyroxin for symptomatic hypothyroidism.

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