Thyroid disease in pregnancy

Thyroid diseases are common in women of childbearing age, so it is not unusual to find a pregnant woman with a thyroid disorder. There is also a close relationship between the thyroid gland and pregnancy. Iodine deficiency, alterations in thyroid function, goitre and changes in autoimmune thyroid disease may be associated with pregnancy.

The changes in thyroid function during pregnancy

Thyroid hormone requirement increases during gestation. The foetus depends on maternal thyroxine in the first trimester for the normal development of brain. Oestrogen stimulates the production of thyroid binding globulin (TBG) leading to an increase in the serum total thyroxine (TT₄) and total triiodothyronine (TT₃). The serum free T₄ (FT₄) and free T₃ (FT₃) remain normal. To maintain the increase in thyroxine production, thyrotropin (TSH) secretion increases. Soon after delivery TSH and thyroid hormone levels return to the pre-pregnant state.

Iodine requirement increases throughout pregnancy because of increased renal loss and diversion to the foetus, and if iodine intake is borderline or low, clinically significant hypothyroidism may develop. WHO recommends a daily intake of 200 μg of iodine in pregnancy.

Human chorionic gonadotropin (hCG) is a weak thyrotropic hormone and may stimulate the thyroid gland and suppress TSH. This effect of hCG becomes clinically important only in women with a sustained elevation of hCG (eg. hyperemesis gravidarum). Changes in the immune system also occur during pregnancy. This influences the course of thyroid disease and predisposes to a relapse or de novo occurrence of autoimmune thyroid disease.

The thyroid problems seen in pregnancy include,

- Hyperthyroidism
- Hypothyroidism
- Postpartum thyroiditis
- Thyroid nodule

Hypothyroidism

Patients with overt and subclinical hypothyroidism require the measurement of FT₄ and TSH at the antenatal booking, each trimester and 2-4 weeks post-partum. As the thyroxine requirement increases in pregnancy, women already on thyroxine replacement need a 25-50% increase in the dose. Women with subclinical hypothyroidism may become hypothyroid and require treatment. The aim is to maintain an euthyroid state with the FT₄ at the upper limit and TSH at the lower limit of the reference ranges. After delivery, the thyroxine dose could be reduced to the pre-pregnant level.

Box 1. Hypothyroidism in pregnancy – summary of management

Pre-pregnancy
- Delay pregnancy till euthyroid and a maintenance thyroxine dose is achieved

Prenatal
- Measure thyroid function (TSH and FT₄) each trimester (every 4-6 weeks till biochemically stabilised)
- Continue full thyroxine replacement (may need to increase the dose by 25-50%)

Labour and delivery
- No specific management

Postnatal
- Check thyroid function 2-4 weeks post-partum, and reduce thyroxine to pre-pregnant doses

Hyperthyroidism

Hyperthyroidism is mostly associated with Graves disease and may be exacerbated in the first trimester due to the stimulatory effect of hCG. Generally there is an improvement in the second and third trimesters because of maternal immunosuppression. About 50% of women with Graves disease have a postpartum relapse.

The patient may present with goitre, symptoms and signs of thyrotoxicosis, ophthalmopathy, or other features associated with Graves disease. The two most serious maternal complications associated with uncontrolled thyrotoxicosis are heart failure and thyroid storm. Fetal risks in hyperthyroidism include spontaneous abortion, preterm delivery, stillbirth, low birthweight and neonatal thyrotoxicosis. Hence it is important to render the patient euthyroid before and during pregnancy.
Management

Antithyroid drugs (propylthiouracil, carbimazole) are the mainstay of treatment and the aim is to make the patient euthyroid. Antithyroid drugs cross the placenta and are secreted in breast milk. Carbimazole can rarely cause aplasia cutis and enter breast milk more than propylthiouracil (PTU), making PTU the drug of choice. The drug dose should be reduced to a minimum sufficient to maintain the FT4 at the upper limit of the reference range. This is especially important in the first trimester, where even mild hypothyroidism can cause foetal hypothyroidism or goitre. As higher doses of antithyroid drugs are used in a ‘block and replacement’ regimen, patients already on this treatment regimen should immediately be converted to antithyroid medication only. The usual daily maintenance dose of carbimazole is 5mg and of PTU is 50mg. Treatment may be stopped towards term if the patient is euthyroid.

β blockers are indicated if the patient has severe thyrototoxicosis, but their use is limited to a short period as they can cause intrauterine growth retardation (IUGR), small placenta, foetal bradycardia and hypoglycaemia.

Thyroidectomy is reserved for patients who are intolerant of antithyroid medication, and best done in the second trimester. The patient should be made euthyroid and symptoms of toxicity should be controlled before surgery. Radioactive iodine is contraindicated during pregnancy and up to 6 months post-partum.

Maternal and foetal monitoring

Diagnosis and management of thyroid disease in pregnancy require the estimation of both TSH and FT4 because of changes in TBG, TT4 and TSH that occur during pregnancy. When hyperthyroidism is diagnosed, FT4 should be tested frequently (e.g. monthly) until euthyroid state is stabilised. Women who have been previously successfully treated for hyperthyroidism should have FT4 checked at the antenatal booking and in each trimester. All patients treated for hyperthyroidism should be tested after delivery because of the possibility of a post-partum relapse.

TSH receptor antibody testing at antenatal booking is useful in women with suspected or treated Graves disease, and need not be repeated if low. When maternal antibody titres are elevated, there is a high chance of developing foetal or neonatal thyrototoxicosis.

During antithyroid drug treatment, the foetus should be checked for hyper- and hypothyroidism with foetal heart rate, and ultrasonography for foetal growth and goitre.

Box 2. Hyperthyroidism in pregnancy – summary of management

Prepregnancy
- Establish the diagnosis of hyperthyroidism
- Counsel regarding therapy, maternal and foetal risk, need for regular checks during pregnancy

Prenatal
- Estimate thyroid function monthly till euthyroid (TSH and FT4), then less frequently
- Continue antithyroid drugs (preferably PTU) to maintain clinical and biochemical euthyroidism (FT4 at upper limit of normal range)
- For symptoms of severe toxicity use short term β blockers
- Serial ultrasonography to detect IUGR and goitre in foetus

Labour and delivery
- No specific management

Postnatal
- Watch for worsening symptoms if Graves disease suspected
- Estimate thyroid function 2-6 weeks postpartum and adjust antithyroid therapy accordingly
- Evaluate the neonate for goitre and transient hyperthyroidism

Post-partum thyroiditis

This is a lymphocytic thyroiditis found in 5-18% of women 2-6 months postpartum, in iodine replete areas. It is self-limiting, with a brief thyrototoxic phase followed by transient hypothyroidism. The patient may present with non-specific symptoms (e.g. anxiety, tiredness, depression) and may have a small painless goitre. Such patients should have their TSH and FT4 measured. Thyroid peroxidase antibodies (TPOAb) are usually positive and the detection of (TPOAb) in early pregnancy predicts a 30-50% chance of developing postpartum thyroiditis.

The thyrototoxic phase requires no treatment, but may need to be differentiated from Graves disease. This can be done by the isotope uptake scan showing a low uptake, but breastfeeding has to be temporarily withheld. The hypothyroid phase may require thyroxine therapy in a symptomatic patient. More than 90% of patients recover completely.
Thyroid nodule

Most goitres developing in pregnancy are diffuse, so if a solitary nodule develops pregnancy it is more likely to be malignant. As radioisotope studies are contraindicated in pregnancy, it should be evaluated with ultrasonography and fine needle aspiration. Pregnancy usually does not affect the prognosis of a primary thyroid malignancy.

Recommended reading*


(* These references are for all four articles)

Piyusha Atapattu, MD (Colombo), MRCP (UK). Senior Lecturer in Physiology, Faculty of Medicine, Colombo 8.
e-mail: <piyushaatapattu@yahoo.com>. Competing interests: none declared.