

## HYPERTHYROIDISM IN PREGNANCY

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### Summary

- Thyroid diseases are common in women, including at the time of pregnancies.
- Many typical features of hyperthyroidism are common in normal pregnancies and this may delay or mask the diagnosis.
- Uncontrolled thyrotoxicosis increases the rate of miscarriage, intrauterine growth restriction (IUGR), premature labour and perinatal mortality.
- Multi-disciplinary efforts are required to achieve optimal control of thyrotoxicosis.
- Anti-thyroid drugs are safe and should be used with the lowest possible doses.
- Radioiodine treatment is contraindicated during pregnancy and lactation.
- Indications of surgery include: compression symptoms, thyroid malignancy, non-compliance to medications or when the patient develop drugs side effects

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Thyroid diseases affect 1-2% of women in the reproductive age. Not unexpectedly, thyroid problems are common in women who are pregnant. However, hyperthyroidism complicates about 1-2 in 1000 pregnancies.<sup>1,2</sup> About 50% of the affected women have a positive family history of autoimmune thyroid disease.<sup>3</sup> In this article we will view pregnancy broadly to include the pre-conception, antenatal, intrapartum and postpartum periods, considering both the baby's and mother's well being as equally important.

### Clinical considerations

Many of the typical features of hyperthyroidism are common in normal pregnancy, i.e. palpitations, tachycardia, heat intolerance, emotional liability, hyperemesis gravidarum and goitre. The most discriminatory features of hyperthyroidism in pregnancy are persistent tachycardia, weight loss, systolic flow murmurs, tremor, lid lag and exophthalmos.

### Spectrum of hyperthyroidism in pregnancy

Graves' disease constitutes 95% of hyperthyroidism cases in pregnancy.<sup>4</sup> Most of the distinctive features of hyperthyroidism may be present but the diagnosis of this disease is generally based on an elevated free thyroxine (FT4) level and suppressed thyroid-stimulating hormone (TSH). Other rare causes of hyperthyroidism during pregnancy includes: toxic multi-nodular goitre, toxic adenoma or occasionally trophoblastic diseases, sub-acute thyroiditis, iodine, amiodarone or lithium therapy.

### Diagnosis

Most pregnant women with hyperthyroidism would have already been diagnosed prior to pregnancy. If not, clinical diagnosis can be confirmed by finding deranged thyroid function test (TFT).

### Effect of pregnancy on hyperthyroidism

Thyrotoxicosis often improves during pregnancy, especially in the second and third trimesters (as with other autoimmune conditions due to the immunosuppression in pregnancy). The level of thyroid stimulating antibodies (TSH receptor-stimulating antibodies) may fall with consequent improvement in Graves' disease and a lower requirement for anti-thyroid treatment.<sup>2</sup> However exacerbations may occur in the first trimester, possibly related to human chorionic gonadotrophin (hCG) production and also in the puerperium due to a reversal of the fall in antibody levels seen during pregnancy.

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### **Effect of hyperthyroidism on pregnancy**

Severe and untreated thyrotoxicosis is associated with inhibition of ovulation, menstrual irregularities and infertility. Those who do become pregnant and remain untreated have a significant increased rate of miscarriage, intrauterine growth restriction (IUGR), premature labour and also higher risk of perinatal mortality.<sup>3</sup> For women with mild hyperthyroidism and those with good control by anti-thyroid drugs, the maternal and foetal outcomes are usually good and unaffected by the disease. Poorly controlled thyrotoxicosis may lead to thyroid crisis (storm) and heart failure, particularly at the time of delivery.

### **Effects on foetus and newborn**

Carbimazole, and to a lesser extent, propylthiouracil (PTU), cross the placenta and in high doses may cause foetal hypothyroidism and goitre. None of them is teratogenic, although carbimazole occasionally causes a scalp defect called aplasia cutis.<sup>6,7</sup> Approximately 1% of pregnant women with Graves' disease will give birth to a child with thyrotoxicosis. In most cases this is a transient condition.<sup>6</sup>

### **Management of hyperthyroidism**

#### *Preconception counseling*

Routine preconceptional counseling is very important. The treatment of thyrotoxicosis should be optimised with the lowest dose of effective treatment. The woman should be informed that the anti-thyroid drugs are not teratogenic and safe to be used in pregnancy, discontinuing treatment may lead to a higher risk of mortality and morbidity to both of them. Anti-thyroid drug could be discontinued if the patient has been euthyroid both clinically and biochemically.

#### *Antenatal and intrapartum management*

The optimum care for pregnant women with hyperthyroidism can only be achieved by combined efforts between the family physician and the hospital specialists (obstetrician/ physician/surgeon). The drug usage should be guided by the patient's clinical condition and her thyroid function tests. The aim of treatment is to achieve control of thyrotoxicosis as rapidly as possible and maintain optimal control with the lowest dose of anti-thyroid medication. The woman should be clinically euthyroid, with a free T4 at the upper end of normal range. PTU up to 150 mg/day or carbimazole below 15 mg/day are unlikely to cause problems to the foetus.

Propranolol is often being used in the early management of thyrotoxicosis or during relapses to improve sympathetic symptoms of tachycardia, tremor and sweating. Doses up to 40 mg tds for short periods

are not harmful to the foetus.<sup>8</sup> As the condition improves, doses can be reduced gradually.

Serial ultrasound scan to check fetal growth, heart rate and fetal neck (for goitre) is advisable, especially in those mothers with poorly controlled or newly diagnosed thyrotoxicosis.<sup>3</sup>

Foetal thyrotoxicosis is an uncommon condition. If the condition develops in utero, it may present with foetal tachycardia, IUGR or goitre. Without treatment, the mortality rate may reach 15%.<sup>3</sup> Other fetal complications such as fetal goitre are unlikely.<sup>2</sup> Most women with hyperthyroidism in pregnancy are well controlled. Spontaneous vaginal delivery should be the mode of choice. Caesarean section should be reserved for obstetric indications.

#### *Postpartum management*

The mother should be encouraged to breastfeed her baby. Only 0.07% of PTU and 0.5% of carbimazole doses are excreted in the breast milk and consumed by the breast-fed baby.<sup>9</sup> It is therefore safe to continue treatment and breast-feeding provided not exceeding the above-mentioned doses. Radioiodine therapy is contraindicated in pregnancy and breast-feeding since it is taken up by the foetal/newborn thyroid and may result in thyroid ablation and hypothyroidism.<sup>9</sup>

#### *Management of thyroid storm (crisis)*

Thyroid crisis or storm is a rapid worsening of the thyrotoxicosis brought about by stresses such as infection, labour, caesarean section or any other type of surgery. It affects 1% of pregnant women with hyperthyroidism and associated with a mortality rate of 20-30%.<sup>11</sup> The diagnosis is clinical and suspected when there is history of hyperthyroidism and recent exposure to stress. Features include hyperpyrexia, neurological and psychological disturbances. Management includes close monitoring, hydration (with intravenous fluid), control of fever (with cold sponging and paracetamol),  $\beta$ -blocker (oral or iv propranolol), anti-thyroid drugs and corticosteroids.

#### *Surgery for hyperthyroidism in pregnancy*

Thyroid surgery in pregnancy may be indicated occasionally. Indications include: large toxic goitre with compression symptoms (dysphagia or stridor), confirmed or suspected malignancy, non-compliance to medications or development of drugs allergies or other side effects. Surgery can be safely performed in the second or early third trimester.<sup>12</sup>

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