Aneurin Bevan University Health Board

Hyperthyroidism and Hypothyroidism in Pregnancy Guideline

N.B. Staff should be discouraged from printing this document. This is to avoid the risk of out-of-date printed versions of the document. The Intranet should be referred to for the current version of the document.

Contents:

1. Introduction/Overview

Thyroid disease is common in women of childbearing age. Optimal management of thyroid disease in pregnancy reduces maternal, fetal and neonatal morbidity and mortality.

2. Policy Statement

The Health Board is committed to providing evidence-based, safe care for all pregnant women, in order to optimise outcomes. This document is designed to support safe and effective practice.

3. Aims/Purpose

To provide support for clinical decision making.

4. Objectives

To ensure all of the following for women with thyroid disease in pregnancy:

- Early identification
- Optimisation of treatment
- Appropriate monitoring of thyroid function
- Appropriate monitoring of maternal and fetal wellbeing
- Provision of evidence-based information to women and their care providers

5. Scope

This guideline applies to all clinicians working within maternity services.

6. Roles and Responsibilities

All clinicians working within maternity services are responsible for ensuring implementation of this guideline for women in their care.

7. Guidance

7.1 Thyroid Physiology in Pregnancy

Thyroid function is altered in pregnancy due to increased metabolic requirements.
In the first trimester, HCG is also expected to stimulate the Thyroid Stimulating Hormone (TSH) receptor, which leads to an appropriate fall in TSH in the 1st trimester with associated transient rise in free T4 levels in the first trimester.
Thyroxine binding globulin (TBG) rises throughout pregnancy which leads to an increase in total T4 levels. The change in serum free T4 and T3 is less obvious.
Overall, TSH tends to be lower than usual with a transient rise in free T4 levels during the 1st trimester. TSH then normalises for the rest of pregnancy, and there is a modest fall in Free T4 in 2nd and 3rd trimester, but still within normal range.

Sufficient iodine intake (200mcg/day) during pregnancy and lactation is necessary to meet the need for increased thyroid hormone production and provide iodine to the fetus and neonate.
There is also increased excretion of iodine in the urine during pregnancy due to increased glomerular filtration rate.
Dairy products and white fish are the best dietary sources of iodine so vegans are at increased risk of deficiency and should be advised to take a supplement; some pregnancy multivitamins contain iodine.
In cases of iodine deficiency, the thyroid hypertrophies in order to trap more iodine, which may cause a visible goitre.

T4 can cross the placenta but its passage is unpredictable.
T3 and TSH do not usually cross the placenta.
Thyroid stimulating antibodies (TRAbs), Thyroid reducing hormone (TRH), Thyroid stimulating hormone(TSH) receptor antibodies, propyl thiouracil, carbimazole and iodine cross the placenta.

The fetal thyroid axis functions from 10 weeks gestation. After 12 weeks the fetal thyroid concentrates iodine at a higher rate than the maternal thyroid hence iodine should be avoided.

7.2 Thyroid Function in Hyperemesis Gravidarum

Transient biochemical hyperthyroidism (elevated T4 and low TSH) may occur in up to 11% of women in early pregnancy. This is particularly common in those with hyperemesis gravidarum (HG) due to TSH receptor stimulation by high levels of hCG. These women are rarely symptomatic, and this transient hyperthyroidism is not associated with adverse pregnancy outcomes. Treatment with anti-thyroid medications is therefore not recommended, but if symptoms are present Beta blockers can be used. This transient hyperthyroidism usually resolves by 18 weeks of pregnancy.

A detailed history should be taken for any other symptoms of hyperthyroidism and Thyroid function tests (TFTs) should be interpreted with caution. Patients with transient hyperthyroidism associated with HG will usually have no history of thyroid disease & no goitre. If there is any doubt as to whether abnormal TFTs may be related to HG or Graves' disease, check TSI; this should be negative in transient hyperthyroidism and a positive result requires referral to medical ANC.

Women on Thyroxine with nausea and vomiting in pregnancy should be advised of the importance of continuing to take their Thyroxine daily and should be prescribed antiemetic medication where necessary to achieve this.

7.3 Hyperthyroidism in Pregnancy

Hyperthyroidism has an incidence of 1 in 2000 pregnancies. 95% of these cases are due to autoimmune thyrotoxicosis (Graves' disease). Other causes include a toxic nodule or toxic multinodular goitre, subacute thyroiditis, Hashimoto's thyroiditis and trophoblastic disease. Symptoms may improve during pregnancy, and relapse postnatally.

Thyroid function tests in hyperthyroidism show decreased TSH and elevated T4 or T3.

The risks of maternal hyperthyroidism are primarily associated with uncontrolled thyrotoxicosis. Maternal complications of untreated thyrotoxicosis are heart failure caused by the myocardial effects of T4 and made worse by preeclampsia, infection or anaemia causing Thyroid Storm. This is a medical emergency.

The therapeutic aim is to achieve euthyroid state as early as possible in pregnancy (or ideally, pre-conception) as this minimises the chances of maternal or fetal complications.

Maternal hyperthyroidism is associated with increased risk of miscarriage, growth restriction and stillbirth: The risk is higher if disease presents in pregnancy, long history of Graves' disease, maternal age < 20 years and the disease is poorly controlled.

Neonatal thyrotoxicosis occurs in up to 10% of cases of Graves' disease. This is due to the Thyroid receptor antibodies Thyroid stimulating immunoglobulin (TSI)/TSH receptor antibodies (TRab) crossing the placenta to stimulate fetal thyroid gland and is proportional to the antibody titre.

Presence or absence of Thyroid peroxidase antibodies (TPO) does not alter the maternal or neonatal outcome.
Subclinical hyperthyroidism (low TSH with normal levels of T4) is not associated with any adverse pregnancy outcomes and treatment is not recommended.

Preconception Care
Aim for good control on lowest dose of antithyroid medications which keeps T4 in upper end of normal range (ideally PTU but see considerations below). Many women are under the care of endocrinologists.
Antenatal Care
Book into Combined Medical ANC: RGH - Monday pm; NHH - Tuesday am. These women will also see the endocrine specialists linked to the medical ANC. TFTs should be taken at booking and at least 6-weekly thereafter (as per the endocrinologist advice). Antithyroid medication will be titrated to keep free T4 at the upper end of non-pregnant range. TSI titre should be checked at booking and 28 weeks in all women with current / history of hyperthyroidism. For all women with a positive TSI: • Monitor fetus for growth and goitre by serial USS. • Arrange for weekly check of fetal heart rate (due to risk of tachycardia) - can be done by community midwife. • Send neonatal alert to Dr. Sue Papworth, Neonatologist
Intrapartum Care
No alterations to normal obstetric led care if hyperthyroidism is well controlled. In poorly controlled hyperthyroidism there is a risk of thyroid storm / crisis, which is a medical emergency.
Postnatal Care
Patients should be advised to continue their current medications and have TFTs checked via GP at 6 weeks postnatally. If antithyroid medications have been reduced or stopped in pregnancy, most women will need to restart or increase these in order to avoid a relapse.
Neonatal Care
Neonatal team need to be informed of delivery and should examine the baby. Baby should be observed on the ward for 48 hours and will need a blood test for TFTs at age 5-10 days.

Treatment of Hyperthyroidism

Anti-thyroid drugs: Pharmacological agents Propylthiouracil (PTU) and Carbimazole are both used in pregnancy. PTU has a double action, blocking thyroxine synthesis and the conversion of T4 to T3. Carbimazole blocks thyroxine synthesis. Both may have an immunosuppressive effect. Both are associated with side effects in 2-3% of cases, including rash, fever, agranulocytosis (0.2%) and occasional gastrointestinal side effects. Both cross the placenta and can cause transient neonatal hypothyroidism. 'Block and Replace' regimes (of thyroxine plus antithyroid drug) are therefore unsuitable for pregnant women, as the T4 replacement does not predictably cross the placenta.

Because of a possible risk of teratogenicity with carbimazole literature would suggest its avoidance in the 1st trimester.
There are no known long term developmental effects with PTU exposure in utero. However, PTU is associated with an increased risk of maternal hepatotoxicity compared to Carbimazole. We therefore recommend that patients seeking pregnancy and throughout the first trimester are treated preferentially with PTU. If they require ongoing treatment with antithyroid drug, this may be switched to Carbimazole in the 2nd trimester. After initial stabilisation the dose is reduced as rapidly as possible (and is frequently withdrawn by the 2nd trimester) to achieve a Free T4 at the upper limit of the normal range (this will be managed in the endocrinology clinic).

Both PTU and Carbimazole, appear safe in breast feeding up to doses of 300mg PTU and 15mg Carbimazole. Neonatal effects are rare, but infant TFTs should be monitored. Carbimazole is excreted at concentrations equivalent to the maternal circulation. PTU concentration is only 10% of the maternal circulation, and so is preferable in most cases during this period, though again consideration should be given to the higher potential maternal hepatotoxicity with PTU compared to Carbimazole.

Radioactive iodine is contraindicated in pregnancy and not advised in the 6 months prior to pregnancy for women.

Surgery for thyrotoxicosis is rarely performed in pregnancy, but is not contraindicated, and is usually best timed in the second trimester.

However, the most important principle is good control of hyperthyroidism; pregnancies where there is poor control are more likely to result in complications than those well controlled on either drug. The decision to start, stop or change antithyroid medication should therefore be made in consultation with the patient, by the endocrinologist, ideally in Medical ANC.

Beta Blockers (Propranolol) are used for symptom control such as tachycardia, palpitations or tremor. Long term use can lead to fetal growth restriction, and this should be monitored with serial USS. However, where significant symptoms exist, benefits of beta blockade usually outweigh this risk.

Rare complications-

1) Fetal hyperthyroidism

All women with positive TSI should have serial fetal ultrasound scans. Any of the following features on USS should raise the suspicion of fetal thyrotoxicosis:

- Fetal tachycardia > 170
- IUGR
- Fetal goitre
- Accelerated bone maturation.
- Signs of congestive cardiac failure
- Hydrops fetalis

The presence of any of these features requires urgent MDT assessment and planning including input from an obstetrician, endocrinologist, fetal medicine Consultant, neonatologist and anaesthetist.

2) **Thyroid Storm** (also referred to as thyrotoxic crisis)

This is a rare, sudden and life-threatening condition in pregnancy. It could be seen in undiagnosed or poorly controlled hyperthyroidism. This sudden flare-up of symptoms can be precipitated by labour, infection or surgery.

Symptoms and signs include fever, tachycardia out of proportion to the fever, hypertension, high output cardiac failure, restlessness, coma, seizures, gastrointestinal symptoms: pain, diarrhoea, vomiting, and jaundice.

Thyroid storm is a medical emergency and is associated with high mortality. Rapid diagnosis and aggressive treatment are key.

Principles of Management:

- TFTs should be taken prior to treatment.
- Admission to HDU or ITU setting.
- Multidisciplinary care, including review by the Endocrinology Registrar / Consultant
- Treatment is with high doses of PTU or carbimazole and potassium iodide or sodium iodide (to suppress T3 & T4 production)
- High dose IV Dexamethasone (to block peripheral conversion of T4 to T3)
- Propanolol (to control tachycardia - use with caution if any suspicion of heart failure)
- Phenobarbital (to increase metabolic elimination of T4)
- Supportive therapy with IV fluids, oxygen and antipyretics should be administered.
- Avoid delivery during thyroid storm where possible – stabilise patient first.

7.4 Hypothyroidism in Pregnancy

In the UK hypothyroidism occurs in 2.5% pf all pregnancies, but only 1-3/ 1000 of pregnancies are complicated by overt hypothyroidism. The commonest causes of hypothyroidism are primary hypothyroidism, Hashimoto's thyroiditis. Women can be hypothyroid following thyroid surgery or post I131 therapy.

Hashimoto's thyroiditis is associated with thyroid peroxidase antibodies and antithyroglobulin antibodies.

Primary hypothyroidism is caused by iodine deficiency however this is less likely in the west due to dietary iodine supplementation.

Overt hypothyroidism causes reduced fertility, and an increased rate of 1st trimester miscarriage. This should therefore be corrected prior to conception. If pregnancy does occur it can be associated with pre-eclampsia, raised BP and pre-term delivery. Neuropsychological and cognitive impairment have also been reported in infants born to mothers with overt hypothyroidism.

Subclinical hypothyroidism refers to an elevated TSH but with a normal free T4. This is more common, but though the risks listed above are lower, they may still be present.

Preconception Care

These women are usually under the care of GPs. TSH in the normal range signals adequate replacement therapy.

Antenatal Care

These women are looked after in the general obstetric clinics.
At booking, check TFTs and confirm there is NO past history of hyperthyroidism.

If there is a new diagnosis of hypothyroidism in pregnancy, Thyroxine treatment should be initiated urgently at 1-2microgram/kg/day then TFTs repeated in 6 weeks. TPO antibodies should also be checked.

TFTs should be checked once every trimester, and 4-6 weeks after any change in dose of Thyroxine. Thyroxine should be titrated to maintain serum TSH concentration not more than 2.5mU/l throughout all trimesters of pregnancy.

Guide to alteration of dose of thyroxine

Serum TSH (mU/l)	Increase in thyroxine (µg/day)
2.5-10	25 - 50
10- 20	50 -75
>20	100

Thyroxine should not be routinely increased in pregnancy without checking TFTs first, as there is some evidence that excessive thyroxine could be harmful.

There is no need for regular growth scans unless there is another clinical indication.

Intrapartum Care

No alterations to normal care required in labour.

Postnatal Care

Following delivery, the patient should be advised to resume her pre-pregnancy dose of Thyroxine (as long as hypothyroidism was well controlled prior to pregnancy). TFTs should be checked 6-8 weeks postpartum with GP.

Neonatal Care
In patients with primary hypothyroidism, no alterations to normal neonatal care are required. Most of these patients will not have had TSI routinely checked and should be treated as TSI negative, i.e. normal postnatal care with no additional testing for the neonate.

7.5 Post-Partum Thyroid Dysfunction

Transient thyroid dysfunction occurs in about 5-10% of women. The incidence is higher in women with existing endocrinological disease, eg IDDM. Classically there is transient hyperthyroidism, at 6-12 weeks postpartum followed by hypothyroidism. 80% resolve in 6-9 months. Some need long term thyroxine replacement. This should be managed by endocrinologists.

7.6 Thyroid nodule & Carcinoma of thyroid

Carcinoma of the thyroid may occur in women of childbearing age, and often presents with a thyroid nodule. Urgent referral should be made to the endocrine clinic. FNA for cytology of a nodule >1cm should be performed in pregnancy. Long term thyroxine replacement therapy in the patient with previous thyroid carcinoma is made on an individual case basis but frequently with a suppressed but detectable TSH.

8. Resources

All necessary resources are already available within the Health Board.

9. Training

Staff are expected to access appropriate training where provided.
Training needs will be identified through appraisal and clinical supervision.

10. Implementation

The recommendations in this guideline are already in clinical practice within the Health Board.

11. Further Information Clinical Documents

The evidence for this document has been checked against relevant guidelines provided by RCOG and NICE. A full list of references is included below.

12. Health and Care Standards Wales

This guideline complies with the Health and Care Standards Wales by providing guidance to support the provision of high-quality safe healthcare. This guideline promotes practice that is up to date, effective and consistent and can be used in day-to-day practice to encourage a consistent level of quality and safety across the Health Board. It supports a patient-centred approach, enabling women to contribute to and be involved in decisions regarding their own health and wellbeing.

13. Equality

This policy has undergone an equality impact assessment screening process using the toolkit designed by the NHS Centre Equality & Human Rights. Details of the screening process for this policy are available from the policy owner.

This policy promotes multidisciplinary working between all those involved in the care of women with thyroid disorders in pregnancy.

14. Environmental Impact

An Environmental Impact Assessment has not been carried out for this policy.

15. Audit

It is advised that the recommendations in this document be audited to ensure compliance by all staff.
Auditable standard

16. Review

17. References

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Appendix 1:
Management of Babies with Maternal History of Thyroid Disease