Management of Thyroid Disease in Pregnancy (Maternity)

Guideline

This document can only be considered current when viewed via the Trust intranet. If this document is printed or saved to another location, you are advised to check that the version you use remains current and valid, with reference to the review due date

Document Author	Isy Douek & Sesha Pramodh, Consultant Endocrinologists, Claire Lovelock & Krishna Murala, Consultant Obstetricians, Raquel Alves, Clinical Pharmacist		
Lead Owner	Isy Douek, Consultant Endocrinologist		
This Version	V2	**Status**	Final
Replaces	V1 (13 Sept 2017)		
Approval Date	14/04/2021	**Where**	Maternity Guideline Group (MGG)
Ratification Date	N/A	**Where**	N/A
Date of issue	21/04/2021	**Review date**	21/04/2024
Applies to	Maternity Services	**Exclusions**	

CONTENTS

KEY POINTS

- Women with untreated or poorly-controlled hypothyroidism have increased risk of pregnancy loss, premature birth, low birth weight, and cognitive and intellectual impairment in the offspring.

- Women with untreated or poorly-controlled hyperthyroidism have increased risk of miscarriage, IUGR, preterm labour, perinatal mortality and maternal death. If the woman has Grave's disease, transient neonatal thyrotoxicosis can occur in up to 10% of neonates due to transplacental passage of TSH receptor stimulating antibodies (TRAB).

- If thyroid function is well controlled from early pregnancy the maternal and fetal outcome is usually good.

1.0 PHYSIOLOGICAL CHANGES OF PREGANCY

Early pregnancy: TSH levels fall due to increase in hCG which directly stimulates the TSH receptor. FT4 and FT3 levels rise slightly but remain in the normal range.

2nd and 3rd trimesters: TSH levels rise slightly to within the normal range. FT4 levels drop gradually.

During pregnancy both TSH and FT4 levels should be measured and trimester specific FT4 reference ranges should be used. These are available on all laboratory reports.

We also advise that, in women with treated thyroid disease, TSH levels should be maintained in the lower half of the reference range to no more than 2.5mU/L during pregnancy.

2.0 THYRIOD FUNCTION IN THE FETUS

2.1 During the first trimester, maternal thyroid hormones are the only source of thyroid hormones for the fetus.

Fetal TSH appears from 10-12 weeks of pregnancy but there is little thyroid hormone synthesis until week 18-20 of pregnancy.

TSH receptor antibodies can cross the placenta and stimulate the fetal thyroid.

3.0 IODINE AND SELENUIM SUPPLEMENTATION

3.1 Iodine is essential for thyroid hormone production. Women who are planning a pregnancy, pregnant or breastfeeding, should aim for a daily iodine intake of 250mcg.

Supplementation of iodine can be considered with prenatal supplements containing around 150mcg of iodine, in the form of potassium iodide or iodate. The remaining of the requirement should be achieved through diet.

Good sources of iodine include fish, shellfish and dairy products - BDA factsheet has more information on dietary sources of iodine and approximate contents for reference https://www.bda.uk.com/resource/iodine.html.

The total daily iodine intake should not exceed 500mcg, to prevent iodine excess complications, such as fetal thyroid dysfunction. Using seaweed or kelp is not recommended as the amounts of iodine can vary from what is reported and provide excessive quantities of iodine. The use of Lugol's Iodine solution, T3 (triiodothyronine) or thyroid extracts is not recommended.

Women being treated for hyperthyroidism or taking levothyroxine do not need to initiate supplementation, as their hormones levels are being monitored and regulated with medication.

4.0 MANAGEMENT OF HYPOTHYRIODISM (FLOW CHART APPENDIX A).

There is frequently (50-85% of women) a need to increase thyroxine dose during pregnancy, by up to 50% of the pre-pregnancy dose. This increase in thyroxine requirement occurs from 4-6 weeks of pregnancy, gradually increases to 16-20 weeks of pregnancy and then plateaus until delivery. Maintaining super-tight control of hypothyroidism is thought to prevent diminution of IQ in

the fetus.

4.1 WHO AND WHEN TO REFER

- Women with primary hypothyroidism do not need Referral to the Medical Antenatal Clinic unless TFTs are difficult to control.
- We advise Referral to the Medical Antenatal Clinic for women with:
    - A history of thyroid cancer - require different TSH targets and monitoring.
    - Large goitre (need anaesthetic assessment)
    - Previous history of Graves' disease even if previous surgery*
    - Previous treatment with radioactive iodine*
    - Severe hyperemesis (unable to ingest thyroxine therapy)

*These women will need monitoring for fetal & neonatal hyperthyroidism as they may still have TSH receptor antibodies. – see management of hyperthyroidism, antenatal care below.

4.2 PRE-CONCEPTION CARE

- Identification of all women with hypothyroidism (any cause) between the ages of 16 and 45 years. These women should be counselled at their annual medicines review/annual TFT check that there is almost certainly a need to increase the levothyroxine dose in early pregnancy to aid fetal brain development in particular.
- If woman is planning pregnancy she should be advised to have a TFT check.
- Her pre-pregnancy dose should be adjusted to keep the TSH in the lower half of the reference range (i.e TSH 0.34-2.5mIU/L).
- The woman should be advised to avoid conception until her treatment is optimised.
- The woman should also be advised to undertake an urgent pregnancy test if she suspects pregnancy and to make contact with her GP as quickly as possible in pregnancy to have an early TFT. She should also be advised how to make an initial temporary adjustment to her thyroxine dose in pregnancy (see section on antenatal care).
- The need for regular dosing should be explained.

4.3 ANTENATAL CARE (& see flow chart appendix A)

- Women should be guided that when pregnancy is suspected they should undertake a pregnancy test (available at pharmacies) as soon as possible.
- If the test is positive the woman should **immediately increase her dose of thyroxine by 25mcg daily** and medical advice should be sought within seven days. She should continue this practice until instructed otherwise, according to her TFT results when available. The fetus cannot receive too much thyroxine because of placental metabolism – there is no need to worry about short term over treatment.
- At the first contact of the pregnancy arrangements need to be made for the TSH and FT4 to be checked as soon as possible - again within 7 days. The TFT results are available 1 working day later and should be communicated to the woman – each health centre needs to be clear who is to make this contact and when (we appreciate that services differ within Primary Care).
- When this information is available, follow the guide below:
    - TSH 0.34-2.5 – revert back to usual dose of Thyroxine
    - TSH 2.5- 5.0: continue with Thyroxine increase of 25mcg
    - TSH >5.0 : increase Thyroxine by 50mcg
- The daily dose can be adjusted as necessary in steps of 25 - 50mcg thyroxine with the TFTs repeated **4 weeks** later until the target TSH is reached. The aim is to adjust the dose of thyroxine to keep the TSH in the lower half of the reference range (i.e. 0.34 -2.5 mIu/l). A 30-50% rise in levothyroxine is appropriate in the first instance.
    - If the TSH is on target at the initial blood test, the TFTs should be checked every 4 weeks until the 16th week of pregnancy. The dose requirement is usually stable for the rest of the pregnancy. After week 16 if the TSH is on target, TFTs should be checked in each trimester (suggest wks 24 and 34) with a follow-up check on changes to the dose 4 weeks later if further adjustment is required.

4.4 POST PARTUM

- Post-partum the dose of levothyroxine reverts immediately to the **pre-pregnancy dose** unless the TSH was out of range in early pregnancy in which case consider continuing thyroxine at a higher dose (suggest weight based dose of 1.6mcg/kg).
- Check TFTs 8-12 weeks post-partum.

5.0 MANAGEMENT OF HYPERTHYRIODISM

5.1 TYPES OF HYPERTHYROIDISM IN PREGNANCY

- **Gestational transient thyrotoxicosis** –occurs in 1-3% of pregnancies. FT4 elevated and TSH suppressed due to elevated hCG levels. It usually does **not** require anti-thyroid medication because it is mild and subsides as hCG production falls (typically by 14 to 18 weeks gestation). This can be associated with **hyperemesis gravidarum.**
- **Graves' disease -** Most women with Grave's disease will be known to the Endocrine team and on appropriate treatment. A new diagnosis of Graves' hyperthyroidism can occur in pregnancy. The presence of a goitre, opthalmopathy and TSH receptor antibodies will add weight to the diagnosis. Graves hyperthyroidism usually becomes less severe during the latter part of pregnancy**. Refer all women with Graves' disease** to the Medical Antenatal Clinic. If you are unsure of the diagnosis contact Endocrine Consultant for advice.

5.2 PRE-CONCEPTION

- Pregnancy should be postponed until a stable euthyroid state is reached.
- Women should be counselled about the options of definitive therapy and of antithyroid drug therapy as part of preconception care planning. This should be by their Endocrinologist
- Women continuing on antithyroid drug therapy should be advised that Propylthiouracil (PTU) is favoured over Carbimazole in the first trimester. Consider changing to PTU in the pre-conception period.

5.3. ANTENATAL CARE

Women with Graves' disease are seen regularly in the medical antenatal clinic.

- Check TSH & FT4 as soon as pregnancy diagnosed & 4 weekly throughout pregnancy. Aim to maintain FT4 at upper limit of reference range.
- Anti-thyroid medications should be continued & titrated to lowest dose necessary to control thyroid function. This will be done by an Endocrine team member in the Medical Antenatal clinic. General principles are listed below.

- 1st trimester: change to Propylthiouracil (PTU) if on Carbimazole because of the possible association of Carbimazole with congenital abnormalities (2-4%) such as aplasia cutis, choanal or oesophagteal atresia, abdominal wall defects, VSD. This will be done by the Endocrinologist who usually sees the woman and who will refer on to the Medical Antenatal Clinic. Carbimazole 5mg is considered to be approximately equal to 50mg of PTU. Note PTU (2-3%) associated with minor birth defects (face and neck cysts, urinary tract abnormalities) felt to be less severe than Carbimazole associated birth defects.
- Whilst taking PTU monitor LFTs at same frequency as TFTs. This is because there have been rare reports of liver toxicity with PTU treatment. If ALT 3x upper limit of normal, PTU should be discontinued.
- 2nd Trimester: switch from PTU to Carbimazole. This is because the risk of teratogenesis during organ development is past.

- TSH receptor antibodies (TRAB) should be measured at the first visit and and at 28 weeks gestation.
- Women with active Graves' disease (on anti-thyroid drugs) and/or with positive TSH receptor stimulating antibodies will require assessment for fetal thyroid dysfunction
    - Ultrasound scans at 28 & 36 weeks for fetal growth (& goitre if uncontrolled hyperthyroidism)
    - Assessment for fetal tachycardia weekly from 36 weeks
- Inform neonatologists. Set up fetal file for all babies of mothers with Graves' disease, past and present.

5.3 POST PARTUM

- Endocrinology team will guide dose of antithyroid medication post delivery
- It is safe to breast feed on PTU <450mg /day or Carbimazole 20mg/day
- Continue to check TSH & FT4 4-6 weekly
- Endocrine follow up will continue

6.0 South West Regional Consensus on Testing for & Treatment of thyroid dysfunction before and during pregnancy, March 2017

- This guideline is for women who are **NOT** taking Thyroxine & are **NOT KNOWN** to have active thyroid disease.
- The finding of an abnormal TSH during pregnancy does not imply lifelong hypothyroidism

6.1 Who to test

Consider testing for ***TSH & TPO antibodies*** preconception or after a positive pregnancy test if a woman has any of these factors:

- Autoimmune Disease : Type 1 Diabetes, Coeliac Disease, Addisons Disease, Pernicious anaemia
- Taking Lithium
- Goitre
- Past history of thyroid surgery / head or neck irradiation
- Past history of abnormal thyroid biochemistry / thyroid disease
- Past history of postpartum thyroiditis
- Recurrent miscarriage (3 or more)
- Previous unexplained preterm delivery (less than 37 weeks)
- First degree relative with thyroid disease

6.2 Interpretation of result

TPO	TSH	Action: preconception	Action: pregnant	Action: Post partum
Negative	Within laboratory reference range	No treatment required		
	Above laboratory reference range	1. TSH up to 10mIU/L: confirm on repeat test after 2-3 months then start Thyroxine 50mcg od 2. Titrate to achieve TSH 2.5mIU/L or less within reference range	1. TSH up to 10mIU/L: start Thyroxine 50mcg od 2. Titrate to achieve TSH 2.5mIU/L or less within reference range 3. Refer to joint endocrine ANC as per local hypothyroid pregnancy protocol	Stop if family complete. If planning further pregnancy discuss with patient
		1. TSH >10mIU/L: start Thyroxine 75mcg od **or** weight based dose* 2. Titrate to achieve TSH 2.5mIU/L or less within reference range	1. TSH > 10mIU/L: start Thyroxine 75mcg od **or** weight based dose* 2. Discuss with Maternity Endo team 3. Titrate to achieve TSH 2.5mIU/L or less within reference range 4. Refer to joint endocrine ANC as per local hypothyroid pregnancy protocol	Continue lifelong
Positive	2.5mIU/L or less	No treatment required		
	Above 2.5mIU/L & within laboratory ref range	No No treatment required	1. Start Thyroxine 50mcg od 2. Titrate to achieve TSH 2.5mIU/L or less within reference range 3. Refer to joint endocrine ANC as per local hypothyroid pregnancy protocol	Stop if family complete. If planning further pregnancy discuss with patient
	Above laboratory reference range	1. TSH up to 10mIU/L: start Thyroxine 50mcg od 2. Titrate to achieve TSH 2.5mIU/L or less within reference range	1. TSH up to 10mIU/L: start Thyroxine 50mcg od 2. Titrate to achieve TSH 2.5mIU/L or less within reference range 3. Refer to joint endocrine ANC as per local hypothyroid pregnancy protocol	Continue lifelong
		1. TSH >10mIU/L: start Thyroxine 75mcg od **or** weight based dose* 2. Titrate to achieve TSH 2.5mIU/L or less within reference range	1. TSH > 10mIU/L: start Thyroxine 75mcg od **or** weight based dose* 2. Discuss with Maternity Endo team 3. Titrate to achieve TSH 2.5mIU/L or less within reference range 4. Refer to joint endocrine ANC as per local hypothyroid pregnancy protocol	
	2.5 mIU/L or less & recurrent miscarriage	Discuss with Maternity Endocrine team		

* Weight based dose - preconception 1.6mcg/kg/day, pregnant 2mcg/kg/day

Consensus group:

Isy Douek, Musgrove Park Hospital, Taunton
Karin Bradley & Natasha Thorogood, University Hospitals Bristol
Andrew Johnson & Kathryn Lonnen, North Bristol NHS Trust
Kate Evans & Ioannis Dimitropoulos, Derriford
Gill Spyer & Mike Gilroy, Torbay Hospital
Alastair Watt, North Devon District Hospital
Kurien John, Weston General Hospital
Mike Masding, Poole Hospital NHS Foundation Trust
James Lawrence, Salisbury District Hospital
Tony Robinson, Royal United Hospital, Bath
Sally Thrower, Gloucestershire Royal Hospital
Helen Holt, Royal Bournemouth Hospital
Helen Gray, Cheltenham General Hospital
Fiona Wotherspoon, Dorset County Hospital
Bijay Vaidya, Royal Devon and Exeter Hospital
Duncan Browne, Royal Cornwall Hospital
Seshadri Pramodh, Yeovil District Hospital

7.0 REFERENCES

1. Abalovich M. Overt and Sub-clinical hypothyroidism complication pregnancy *Thyroid* 2002 12:63-68
2. Haddow J.E. Maternal thyroid deficiency in pregnancy and subsequent neuropsychological development of the child *New Eng J Med* 1999 341:549-555
3. Chan S. Thyroid hormones in pregnancy and the fetus *Progress in Obs and Gynae* 2003 15:80
4. Alexander E.K. Timing and magnitude of increases in levothyroxine requirements during pregnancy in women with hypothyroidism *New Eng J Med* 2004 351: 241-249
5. De Groot L et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab. 2012;97*(8):2543
6. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum
7. 2018 European Thyroid Association Guideline for the Management of Graves' Hyperthyroidism. *Eur Thyroid J 2018; 7:167-186*
8. Management of thyrotoxicosis during pregnancy. *Best Practice & Research Clinical Endocrinology and Metabolism 2020; 34*
9. Safety of antithyroid drugs in pregnancy: update and therapy implications. *Expert Opinion on Drug Safety 2020; vol 19, No. 5, 565-567*

APPENDIX A - Pregnancy Care for Women with Hypothyroidism

1. History of hyperthyroidism which has been treated & now on thyroxine
2. Hypothyroidism due to previous history of thyroid cancer surgery
3. Pituitary disease

↓

YDH - Joint obstetric and endocrine clinic

MPH- Medical antenatal clinic

Low risk woman with primary hypothyroidism

↓

GP & Community midwifery care

↓

1. Increase thyroxine daily dose by 25mcg as soon as pregnancy confirmed
2. Check TFTs within 7 days if not done within previous 4 weeks

↓

- TSH 0.34-2.5: Revert back to usual thyroxine dose
- TSH 2.5-5: continue with thyroxine increase of 25mcg
- TSH >5: increase thyroxine by 50mcg

↓

Re-check TFTs 4 weekly until 16 weeks then each trimester

Adjust thyroxine dose to achieve TSH 0.34-2.5

↓

Post partum

- Reduce to pre-pregnancy dose at delivery or weight based dose (1.6mcg/kg) if TSH not controlled pre conception
- Check TFTs 8-12 weeks post-natal

✓ Always check that woman is taking her thyroxine before any dose change

✓ Ensure taking thyroxine on an empty stomach (no food/ suppements/ medication or drinks except water for at least 30 mins, ideally longer)