Management of Thyrotoxicosis in Pregnancy- Full Clinical Guideline

Reference no.: UHDB/OBS/06:22/T9

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1. Introduction

Thyroid diseases are the commonest cause of endocrine dysfunction in women of childbearing age and, therefore, encountered commonly in pregnancy. Disorders of thyroid hormone production and their treatment can affect fertility, maternal well-being, fetal growth and development. Whilst hypothyroidism is common, hyperthyroidism has much greater implications for pregnancy.

2. Purpose and Outcomes

Adequately treated hyperthyroid mothers develop few complications and good outcome is expected.

3. Key Responsibilities and Duties

All patients should be referred to the joint endocrine/antenatal clinic as soon as possible for joint care in pregnancy. Transient neonatal hyperthyroidism occurs in less than 2% cases due to transplacental passage of TSH receptor antibody which stimulates fetal thyroid gland. Fetal Ultrasound surveillance and Neonatal alert is essential.

4. Abbreviations

IUGR -- Intrauterine growth retardation
TRAb -- Thyroid stimulating hormone receptor antibodies
PTU -- Propylthiouracil

TFT -- Thyroid function tests
TSH -- Thyroid stimulating hormone
FT4 -- Free Thyroxine
FT3 -- Free Tri-iodothyronine
CBZ -- Carbimazole
ATD -- Antithyroid medication
NICU -- Neonatal intensive care unit
HCG -- Human chorionic Gonadotropin

5. Hyperthyroidism

The most common cause of hyperthyroidism in pregnancy is autoimmune Graves disease which occurs in 0.2% pregnancies. Non-autoimmune conditions such as toxic adenoma and toxic multinodular goitre are less common.
Maternal thyrotoxicosis is associated with miscarriage/stillbirth, IUGR and/or fetal thyrotoxicosis. The latter occurs due to transplacental passage of thyroid receptor antibodies (TrAb) and can present with growth retardation, fetal goitre and tachycardia. The risk of the fetal/neonatal thyrotoxicosis increases with increasing titres of TrAb.

5.1 Pregnant women with current thyrotoxicosis on antithyroid medication (ATD)

a. Propylthiouracil (PTU) is recommended for the treatment of maternal hyperthyroidism through 16 weeks of pregnancy; after 16 weeks of gestation, the therapy should be changed to Carbimazole
b. TSH, FT4 (and often FT3) should be monitored every 4 weeks and the target of treatment is FT4 at the upper limit or just above the reference range
c. Monitor for fetal hyperthyroidism – observe for IUGR – see fetal ultrasound surveillance section
d. If a pregnant woman remains euthyroid on a low dose of PTU or CBZ, a trial off ATD could be considered taking individual risk factors for relapse into account. After stopping ATD, TFTs should be checked 2-4 weekly.

5.2 If history of medically treated hyperthyroidism (currently euthyroid)

a. TFTs every 8 weeks (each trimester)
b. No additional fetal monitoring required
c. Thyroid receptor antibodies testing not required

5.3 If history of surgically treated hyperthyroidism or radioactive iodine treatment (currently euthyroid)

a. TFTs every 8 weeks (each trimester)
b. Thyroid receptor antibodies to be checked early in pregnancy
    i. If absent or low – no need to repeat TrAb titres later in pregnancy; no fetal growth scans required.
    ii. If significantly raised (>5 IU/L at RDH and >2.7 IU/L at QHB) – increased risk of fetal thyrotoxicosis; re-measure at 18-22 weeks, and if still high, repeat again at 30-34 weeks. Observe for IUGR (growth scans at 28-30, 34, 38 weeks), Neonatal alert.

5.4 Gestational transient thyrotoxicosis

It affects 1%-3% of pregnancies, is related to elevated HCG levels and often associated with hyperemesis gravidarum. Careful medical history (prior history of thyroid disorder), physical examination (goitre, orbitopathy) and assessment of FT3, FT4 and TrAb levels help differentiate the aetiology of thyrotoxicosis.

6. Antithyroid medication

Carbimazole and Propylthiouracyl block the synthesis of thyroxine, with PTU additionally inhibiting T4 to T3 conversion. Both drugs are associated with a number of side effects including allergic reactions/rashes, risk of agranulocytosis (0.2%) and acute liver toxicity in the case of PTU.

Carbimazole use in the first trimester has been associated with fetal aplasia cutis and therefore PTU is the preferred agent until 16 weeks of gestation. Thereafter, PTU can be replaced by Carbimazole in view of a lower risk of maternal hepatotoxicity associated with its use.

The blocking replacement regimen should not be used during pregnancy since very little thyroxine crossed the placenta in the last trimester. Breastfeeding is considered safe when maternal doses of Carbimazole and PTU do not exceed 15mg/ day and 150 mg/day, respectively.

Thromboprophylaxis is not routinely indicated for patients with Autoimmune Hyperthyroidism and to be considered if they have other risk factors after discussion with Obstetrician in Antenatal clinic.

7. History of Thyroid cancer

1, Referral to Endocrine clinic: TSH target during pregnancy same as determined preconception

2. TFTs monitoring every 4 weeks until week 20 and once in late 2nd/early 3rd trimester

3. Ultrasound thyroid and thyroglobulin levels monitoring during pregnancy should be performed only in women with a history of a well differentiated thyroid cancer who had evidence of residual or recurrent disease prior to pregnancy; such monitoring is not required if patient was disease-free pre-pregnancy

8. TSH receptor antibodies (TrAb)

TSH receptor antibodies should be checked in 1st trimester in women with:

1 Not yet treated or ATD-treated hyperthyroidism
2. Previous history of Graves' disease treated with either radioactive iodine or total thyroidectomy
3. Previous history of delivering infant with thyrotoxicosis

a) If TrAb is low or undetectable in early pregnancy - no need to measure further.
b) If TrAb is elevated (>5 IU/L at RDH and >2.7 IU/L at QHB- different reference ranges across both sites) TrAb should be remeasured at 18-22 weeks.
If they remain elevated and/or mother continues on ATD in 3rd trimester, TrAb should be rechecked at 30-34 weeks

9. Fetal ultrasound surveillance (includes assessment of fetal thyroid at 28 -30 weeks at Fetal Medicine Unit and growth scans at 34 and 38 weeks) required in women with:

1. Uncontrolled hyperthyroidism in the second half of pregnancy.
2. TrAb > 5 IU/L at RDH and >2.7 IU/L at QHB at any point in pregnancy.
3. Women with non-autoimmune causes of hyperthyroidism (toxic adenoma/ multinodular goitre) Who require ATD during pregnancy.

10. Monitoring Compliance and Effectiveness

As per agreed business unit audit forward programme

1. Booking TFTs Performed
2. TFTS each trimester
3. Anaesthetic review if thyrotoxicosis not controlled
4. Neonatal review

11. Referrals

Royal Derby Hospital- All pregnant women who have Hyperthyroidism should be referred to Joint Antenatal/Endocrine clinic (SUM1T)

Queens Hospital, Burton- All pregnant women who have Hyperthyroidism should be referred to Obstetric consultant with special interest in Endocrinology (Antenatal clinic) and will also get an appointment in endocrine clinic.

12. References

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