Management of thyroid disorders in pregnancy: Recommendations made simple
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Abstract
This review covers the current American Thyroid Association recommendations on diagnosis and management of thyroid disease during pregnancy and the postpartum period. It lists the recommendations in a reader-friendly way, and facilitates rational therapy of thyroid disorders, in relation to obstetric health, at the primary care level.

Keywords: Antenatal, Antithyroid drug, Hyperthyroidism, Hypothyroidism, Thyroid cancer, Thyroid nodules, Lactation.

Introduction
Thyroid disorders are common in India,1 and especially so in women of reproductive age group.2 The vast majority of women with thyroid disease seek treatment from their obstetric care providers. Though endocrinology has made great strides,3 the number of endocrinologists is not sufficient to cater to the needs of South Asia. This review lists current recommendations for management of thyroid disorders in obstetric practice4 in a simple, reader-friendly way. Through this, we hope to achieve optimal thyroid health, and a more intelligent future generation,5 in our region.

Hypothyroidism and Pregnancy
Laboratory Assessment
• TSH (thyroid stimulating hormone) assessment should be based on population based trimester specific reference ranges, calculated from data of healthy pregnant women without h/o thyroid disease, with optimal iodine intake, and negative TPO Ab (thyroid peroxidase antibody) status.
• If pregnancy specific population-based data is not available, URL (upper reference limit) of 4.0 mU/L may be used.
• A level 0.5mU/l lower than non-pregnant URL can also be taken as URL for TSH in pregnancy

- Serum T4 (thyroxin) is a highly reliable marker for thyroid function in last period of pregnancy

Preconception Investigations
• Test TSH in all women presenting with infertility
• Test TSH either before, or 1-2weeks after, controlled ovarian hyper stimulation (COHS)
• Non pregnant women with mild TSH elevation following COHS should undergo repeat testing after 2-4 weeks
• Test TSH at time of diagnosis of pregnancy, in euthyroid, antibody positive women

Iodine Intake
• Ensure iodine intake of 250 µg/day, at least 3 months prior to conception.
• Such intake is not required in women who are on treatment for either hypo or hyper-thyroidism.
• Avoid iodine intake > 500 µg/day.
• Avoid iodine containing supplements in excess

Preconception Counselling
Hypothyroid women on treatment should
• Aim for a TSH between LRL (lower reference limit) and 2.5mU/L
• Contact their endocrinologist/obstetrician immediately if pregnancy is suspected or confirmed
• Increase their dose of LT4 by 20-30% (to 9 tablets per week) as soon as pregnancy is suspected or confirmed.

Preconception Management
• LT4 therapy is recommended in all women with overt hypothyroidism and infertility
• LT4 (25-50 µg/day) can be considered in women with SCH, attempting natural conception.
• LT4 is not recommended in antibody positive, euthyroid women attempting natural conception
• LT4 is recommended in women with SCH undergoing IVF (in vitro fertilization) /ICSI (intracytoplasmic sperm injection), targeting a TSH target <2.5 mU/L.

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**Antenatal Management**
- Routine obstetric care should be performed for all women with thyroid disorders.
- LT4 is recommended during pregnancy for treatment of:
  - Women with overt hypothyroidism
  - TPO Ab +ve women with TSH greater than pregnancy specific URL
- TPO Ab -ve women with TSH > 10mU/l
  - LT4 may be considered for:
    - TPO Ab +ve women with TSH >2.5mU/l
    - TPO Ab -ve women with TSH > pregnancy specific URL.
- 25-50 µg LT4 may be prescribed to TPO Ab +ve, euthyroid pregnant women with history of pregnancy loss
- LT4 is not recommended for TPO Ab -ve women with a normal TSH
- LT4 is not recommended for isolated hypothyroxinaemia.

**Antenatal Monitoring**
The target TSH is lower half of trimester specific reference ranges, or < 2.5mU/l
TSH should be monitored every 4 weeks until midgestation, and at 30 weeks, in women with:
- Overt hypothyroidism
- Subclinical hypothyroidism
- Antibody +ve euthyroidism
- Past h/o hemi thyroidectomy
- Past h/o radioactive iodine therapy
This frequency should be maintained, whether the women is on treatment or not

**Post Partum Management**
LT4 dose should be reduced to preconception dose after delivery
LT4 can be discontinued after delivery if:
- Therapy was initiated during pregnancy
- The dose is <50µg/day
TSH should be evaluated at 6 weeks post-partum, and at regular intervals thereafter

**Complementary Therapy**
- Selenium supplementation is not recommended for treatment of antibody positive pregnant women
- Intravenous immunoglobulin is not recommended for treatment of euthyroid women with RPL.
- Glucocorticoid therapy is not recommended for euthyroid, Ab +ve women undergoing ART
- T3 or desiccated thyroid is not recommended during pregnancy.

**Hyperthyroidism and Pregnancy**

**Preconception Counselling**
- Hyperthyroid women should postpone pregnancy until a stable, euthyroid state (defined as two sets of normal thyroid function, within the reference range, measured at least one month apart, without any change in therapy between tests) is achieved.
- Women on ATD (antithyroid drugs) should confirm pregnancy as soon as possible, and contact their endocrinologist/obstetrician immediately
- Women with severe hyperthyroidism or high TRAb levels should prefer surgery or ATD over RAI.
- RAI (radioactive iodine) should be administered only after a negative pregnancy test
- Conception in women who have received RAI should be delayed for at least 6 months, and until a euthyroid state is achieved with LT4

**Antenatal Management**
- Suppressed TSH, detected during first trimester, should be evaluated for etiology
- Gestational transient thyrotoxicosis and / or hyperemesis gravidarum should be treated with supportive measures, including fluids. Beta blockers may be considered

**Antithyroid Drug Therapy**
- Graves’ disease should be treated with ATD if required, in lowest effective dose.
- PTU (propylthiouracil) is the preferred drug till 16 weeks gestation
- Pregnant women on MMI (methimazole) or CMZ (carbimazole) should be shifted to PTU as soon as possible. Dose may be calculated as
  5mg MMI=100 mg PTU
10 mg CMZ = 120 mg PTU
- Either PTU, MMI or CMZ may be used after 16 weeks gestation
- Target FT4/TT4 (free thyroxin/total thyroxin) should be at or moderately above the reference range
- TSH and FT4/TT4 should be monitored every 4 weeks

**Antithyroid Drug Discontinuation**
ATD may be discontinued during first trimester if:
- Dose requirement is low
- MMI < 5-10 mg/d
- CMZ < 10-20 mg/d
- PTU < 100-200 mg/d
- Duration of ATD treatment is > 6 months
- Orbitopathy or large goiter is absent
- TSH is normal
- TRAb (thyroid receptor antibodies) levels are low
- Regular frequent follow up can be ensured

If ATD is discontinued, the patient should be followed up clinically and biochemically every 1-2 weeks, with TSH, and FT4 or TT4. If she remains euthyroid, frequency of follow up may be reduced to 2-4 weekly during 2nd and 3rd trimesters.

**TRAb Estimation**
TRAb estimation during early pregnancy is indicated in antenatal women with:
- Untreated hyperthyroidism
- ATD treated hyperthyroidism
- Past h/o RAI
- Past h/o thyroidectomy
- Past h/o delivery of infant with hyperthyroidism

TRAb testing should be repeated at week 18-22 if:
- Initial TRAb concentration is elevated (> 5 IU/l, 3x ULN)
- ATD treatment is required

TRAb testing should be repeated at week 30-34 if:
- TRAb concentration is elevated at week 18-22
- ATD treatment is required

**Foetal Surveillance**
Potential foetal hyperthyroidism may be detected on ultrasonography by:
- Foetal tachycardia (> 170 bpm, persistent over 10 minutes)
- IUGR (intrauterine growth retardation)
- Foetal goiter
- Accelerated bone maturation
- Sign of CCF (congestive cardiac failure)
- Foetal hydrops

Cordocentesis or umbilical cord blood sampling is not required in routine practice.

Women receiving ATD for hyperthyroidism due to autonomous nodules should undergo careful foetal surveillance for goiter and foetal hypothyroidism during the second half of pregnancy.

**Thyroid Nodules and Cancer, and Pregnancy Diagnosis**
- A newly detected thyroid nodule with non-suppressed TSH in a pregnant woman should be assessed by ultrasonography and fine needle aspiration if indicated
- A newly detected thyroid nodule with suppressed TSH levels that persist beyond 16 weeks, may be assessed after delivery
- Radioactive iodine uptake and radionuclide scintigraphy should be deferred in pregnant and lactating mothers

**Treatment**
- Pregnant women with cytological evidence of malignant lymph nodes or metastasis, do not require, but may undergo surgery during pregnancy
- Newly detected papillary thyroid carcinoma which remain stable by mid-pregnancy, or is detected in the latter half of pregnancy, may be treated after delivery
- Newly diagnosed medullary carcinoma or anaplastic cancer should be treated without delay.
- Pregnant women with thyroid cancer operated in the past should target their preconception TSH goal (usually < 0.1 mU/l).

**Monitoring**
- TSH should be monitored every week till 16-20 weeks gestation, and at least once at 26-32 weeks
• Ultrasound and thyroglobulin monitoring is indicated in pregnant women with:
  • Well-differentiated thyroid cancer
  • Biochemical or structural evidence of:
    • Residual disease
    • Active recurrent disease
  • Ultrasound monitoring is indicated in every trimester in pregnant women with PTMC (papillary thyroid microcarcinoma) who are under active surveillance.

Post Partum Management of Thyroid Dysfunction

Screening
• All newborns should be screened for hypothyroidism, at 48-96 hours age, by blood spot analysis or other available means
• Women with unexplained poor lactation should have TSH measured
• Lactating mothers should not undergo procedures which require radioactive element administration. If required, 123I and Tc 99m can be used, ensuring that breast milk is discarded for 3-4 and 1 day.
• TSH screening should be considered in women with postpartum depression

Treatment
• Thyroid disorders are not a contraindication to lactation
• SCH and overt hypothyroidism should be treated in lactating women
• Hyperthyroidism should not be treated on the premise that it will influence lactation.
• Lowest effective doses of ATD should be used, if required, to manage Graves' disease.

Post Partum Thyroiditis
• Women with postpartum thyroiditis (PPT) may be treated with beta blockers such as propranolol or metoprolol, in low doses
• Serum TSH should be monitored 4-8 weeks after resolution of thyrotoxic phase of PPT, or if symptomatology changes
• Discontinuation of LT4 therapy should be attempted after 12 months
• Annual surveillance with TSH should be maintained

References