Guidelines Review

Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline

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Recent clinical practice guidelines have been published regarding the management of thyroid disease during and following pregnancy, and since many recommendations are likely to impact on the reporting of laboratory results, it is pertinent to review the recommendations.[1] The published article is 47 pages in length but the first 7 pages provide a useful summary of the recommendations. The panel who reviewed and subsequently jointly published the recommendations consisted of endocrinologists representing the American Association of Clinical Endocrinologists, Latin American Thyroid Society, the Asia and Oceania Thyroid Society, the American Thyroid Association and the European Thyroid Association.

Management of thyroid disease in pregnancy is important because pregnancy results in major changes in thyroid function, plus maternal thyroid disease can adversely affect the pregnancy course and foetal well being. In view of the rapidity of advances in the field of thyroid disease in pregnancy and the fact that pregnant women are cared for by multiple health care professionals, the development of guidelines was timely. Peer reviewed literature over the last two decades was reviewed focusing on original publications and graded using the United States Preventative Services Task Force system, which grades on the basis of the strength of evidence and magnitude of benefit compared to potential harm. Recommendations were separated into sections and each section is referenced. The specific recommendations that will impact on pathology services delivery is reviewed below.

Hypothyroidism and Pregnancy

Both overt and subclinical hypothyroidism can have an adverse impact on the course of pregnancy or foetal development. Therefore, hypothyroidism should be corrected before initiation of pregnancy and the task force recommended adjustment of preconception thyroxine (T4) therapy to reach a thyroid stimulating hormone (TSH) level <2.6 mU/L before conception. Specifically, the task force recommends women with subclinical hypothyroidism (serum TSH above the upper reference limit and free T4 [fT4] within reference limits) should be treated with T4 replacement. This recommendation is based on observational evidence demonstrating that women suffering from overt or subclinical hypothyroidism deliver babies with an average intelligence quotient (IQ) score 7 points below the mean IQ score of children born to healthy women and women on T4 replacement. There were also three times as many children with IQ scores that were 2 standard deviations below the mean IQ of the controls in this study, and untreated hypothyroidism during pregnancy was associated with a threefold increase in learning disabilities. The importance of maternal thyroid hormone replacement is emphasised by the knowledge that the foetal thyroid does not develop until the second trimester of pregnancy and foetal thyroid hormone production does not become optimal until mid-gestation.

T4 treatment should be increased by 4–6 weeks gestation and the increase in dosage may be of the order of 30–50%. If hypothyroidism is diagnosed in pregnancy the T4 dose should be titrated rapidly until a TSH of <2.6 mU/L is attained. Maintaining a serum TSH <3 mU/L is acceptable in the second and third trimesters of pregnancy or alternatively, maintaining TSH within trimester-specific reference limits is appropriate. After delivery, the dose of T4 therapy can be reduced.

Hyperthyroidism and Pregnancy

If a subnormal TSH is detected during pregnancy, hyperthyroidism must be distinguished from normal physiology and hyperemesis gravidarum because of the potential adverse effects on the mother and foetus.

Hyperthyroidism in pregnancy is not rare; estimated prevalence is 0.1–0.4% with Graves' disease accounting for 85% of cases and toxic solitary or multiple nodules plus thyroiditis

accounting for most of the rest. Gestational thyrotoxicosis and hydatidiform molar disease are very uncommon causes.

Postpartum thyroiditis may occur in up to 10% of all pregnancies, usually between six weeks and six months after delivery but can occur up to one year later. Because a hypothyroid phase often follows the hyperthyroid phase and is occasionally permanent, careful monitoring is necessary, as women may be hypothyroid at the time of any subsequent pregnancy.

Gestational thyrotoxicosis presents in the mid to late first trimester, often with hyperemesis. Classical hyperthyroid symptoms are absent or minimal apart from weight loss, which is often the result of malnutrition secondary to vomiting.

Non specific symptoms of hyperthyroidism such as tachycardia, systolic flow murmurs, warm moist skin or tremor may occur normally in pregnancy. Furthermore, human chorionic gonadotropin (hCG) mediates a reduction in TSH, with median values of 0.8 mU/L and lower 95th centile limits below 0.1 mU/L. The increase in thyroid binding globulin (TBG) and fall in albumin with pregnancy can result in changes in total as well as fT4 levels. Approximately 50% of women suffering from hyperemesis have a subnormal TSH and elevated fT4. In this setting assessment of free triiodothyronine (fT3) and TSH receptor antibodies (TRAb) are helpful as 90% of hyperemesis cases have normal fT3 and most cases of Graves' disease will be TRAb positive.

If Graves' disease or hyperfunctioning nodules are diagnosed, propylthiouracil is preferred to carbimazole because of the association with congenital abnormalities with the latter medication. Therapy should be adjusted to maintain maternal fT4 in the upper non-pregnant reference interval.

Postpartum Thyroiditis

Thyroid peroxidise (TPO) antibody positive women and women with type 1 diabetes should have TSH assessed at three and six months postpartum. Universal screening is currently not advocated.

Asymptomatic postpartum women with TSH <10 mU/L can be re-monitored within 4–8 weeks but symptomatic women and those planning a subsequent pregnancy should be treated with T4 therapy.

Screening for Thyroid Dysfunction during Pregnancy

Case finding is recommended in women at high risk of thyroid disease. TSH should be measured in women with a history of thyroid disease, postpartum thyroiditis, thyroid surgery, family history of thyroid disease, goitre, positive TPO antibodies, symptoms or signs of thyroid disease (anaemia, increased cholesterol, hyponatraemia), type 1 diabetes, other autoimmune diseases, infertility, previous head or neck irradiation and history of miscarriage or preterm delivery.

Summary and Critique

The recommendations are extensive and very prescriptive providing advice in all possible situations that could be encountered during and after pregnancy. Difficulties arise for laboratories where the history of pregnancy is not provided and/or other pathology is not requested that could indicate pregnancy status. Where pregnancy status is known or inferred, management is different to a non-pregnant female and should be reflected in laboratory commenting.

Adjustment of T4 replacement to achieve TSH <2.6 mU/L before conception is a pragmatic approach to partially address the problem of the increased requirements of T4 replacement in pregnancy. In reality, most women become aware of pregnancy status after four weeks so simple advice to increase T4 dosage as soon as conception is suspected/confirmed is a simple practical approach.

Appropriate commenting that TSH is commonly subnormal or even suppressed in normal pregnancy is needed. Reflex testing of fT4 in such cases would be helpful. Specific advice regarding the measurement of fT3 and TRAb by laboratories is needed.

Most laboratories have not defined trimester specific TSH intervals, but the application of different ideal limits in pregnant or non-pregnant women on T4 replacement may be logistically difficult.

For women on antithyroid medication advice regarding the therapeutic target for fT4 and/or fT3 is needed in pregnancy. This advice will differ from non-pregnant females on antithyroid medication.

The list of criteria for screening for thyroid disease in pregnancy is extensive and in the author's experience, it is highly likely that most women will fulfil at least one of the criteria listed.

Additional sections on autoimmune thyroid disease and miscarriage, thyroid nodules and cancer plus iodine nutrition in pregnancy are reviewed in the clinical practice guidelines but since each of these sections do not have implications for the reporting of biochemistry results, they have not been summarised in this review.

Suggested Laboratory Comments

The author suggests the following comments for use in laboratories, based on the guidelines:

1. TSH <0.4 mU/L and pregnant
   TSH can be subnormal or suppressed in pregnancy and may not indicate underlying thyroid disease. Suggest check fT4 and consider measuring fT3 and TRAb.

2. TSH >4 mU/L and pregnant
   Borderline increase in TSH can occur following recovery from illness, or with early thyroid failure but in view of pregnancy status, treatment with thyroid hormone replacement should be considered in view of potential effects on foetal health of untreated maternal hypothyroidism. Repeat assessment of thyroid function in each trimester of pregnancy is advised.

3. Considering pregnancy/investigating infertility and on T4
   Suggest adjust T4 dose to achieve TSH <2.6 mU/L if pregnancy planned.

4. On antithyroid medication and pregnant
   Suggest adjust therapy aiming for fT4 and/or fT3 close to the upper reference interval.

Competing Interests: None declared.

Reference

1. Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2007;92:S1-47.