CHAPTER

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Thyroid Diseases in Pregnancy

Padmavathy S Menon

INTRODUCTION

Pregnancy results in hormonal and metabolic alterations. In this chapter, we are going to deal with thyroid disorders in pregnancy and to this end; we need to know the alteration of thyroid functions in pregnancy. The commonest clinical situation faced in clinical practice is Hypothyroidism followed by Hyperthyroidism in pregnancy and their management will be dealt in detail. Other disorders that require treatment are goiter, thyroid nodules and malignancy of thyroid.

THYROID FUNCTION ALTERATIONS IN PREGNANCY

Human chorionic gonadotropin (hCG) levels increase in pregnancy and this stimulates the thyrotropin receptor resulting in increase in T_4 and T_3 and a suppression of TSH. The Thyroid Binding Globulin (TBG) increases in pregnancy due to large amount of Estrogen and also due to sialyation of TBG molecule increasing its half-life. The net result is an elevation of T_4 and T_3 (nearly 2 fold) and a low or suppressed TSH. Hence a low or supressed TSH in pregnancy can be a normal finding.

TFT in pregnancy

TSH: Trimester specific ranges for TSH has been evaluated in many studies and American Thyroid Association ATA (2011) and Endocrine society (2013) on the basis of these studied have suggested the normal values for pregnancy (Table-1).

The individual population norms in pregnancy, if available, should be used for deciding the normal values (as well as laboratories), but this being absent we may follow the ATA/Endosociety recommendations.

T_4 is elevated in pregnancy – the method of estimation being not ideal and many variations in kits, FT_4 is done by many. This too has problems as the ideal measurement of FT_4 is LCMSMS (still a research tool) and hence the combination of T_4 and TSH is used for deciding the management in practice. T_3 is also elevated in pregnancy and of limited value as a test for deciding management of thyroid disorders in pregnancy.

Table 1: Trimester specific TSH values

Trimesters	ATA 2011	Endosociety 2013
I	0.1 – 2.5 mIU/L	≤ 2.5 mIU/L
II	0.2 – 3 mIU/L	≤ 3 mIU/L
III	0.3 – 3 mIU/L	≤ 3 mIU/L

Hypothyroidism in Pregnancy

Most of the times, a TSH is done by the obstetrician and referred for abnormal values. Hence no patient comes with any clinical symptoms suggestive of hypothyroidism. Patient at risk for hypothyroidism are those with a history of thyroid disorder in the past or abortion, goiter, radioactive iodine treatment for toxicosis or a history of neck irradiation.

The adverse effects of hypothyroidism include hypertension, eclampsia, placental abruption, miscarriage, risk of C-section and postpartum haemorrhage. Fetal adverse outcome described in literature are: preterm delivery, low birth weight, increased perinatal and neonatal mortality and neuropsychiatric and cognitive impairment.

Subclinical hypothyroidism (SCH) in pregnancy is diagnosed when the TSH is > 2.5 mIU/L and the FT_4 is normal. There is some difference of opinion regarding treatment. Both ATA and Endocrine society recommend treatment when thyroid peroxidase antibodies are positive, but differ when anti bodies are negative (ATA advocates no treatment). In those where antibodies are positive, the TSH tends to rise on follow up by third trimester and hence treatment by thyroxin is recommended by Endocrine society.

Overt hypothyroidism (OH) is diagnosed when TSH is > 2.5 mIU/L to 10 mIU/L and FT_4 is low (pregnancy specific ranges if available). Generally, treatment with thyroxin is indicated.

Goal of treatment of SCH and OH is to normalise TSH values to trimester specific ranges. The starting dose will depend on the TSH level and can be from 25 – 50 µg/day. TSH should be monitored every 4 – 6 weeks and when TSH remains stable for 2 or 3 successive time monitoring can stop and thyroxin continued till delivery. This usually happens around six months.

If pregnancy occurs in a subject who is already on treatment for Subclinical hypothyroidism (SCH) or Overt hypothyroidism (OH), there is likely to be an increase in dose requirement within 4 – 6 weeks of pregnancy. Hence patients on thyroxin are advised to do TSH and report to endocrinologist/physician as soon as pregnancy is detected and the dose revised and followed up as above. After delivery – she goes back to her pre-pregnancy dose.

Positive thyroid antibodies (anti TPO) and pregnancy loss is a matter of controversy as some studies showed

an association and some did not. A meta-analysis of 10 studies showed a clear positive association. However causality is not determined.

Certain unanswered questions remain: (1) should we screen all pregnant thyroid patients? some studies favour and some do not. I personally feel all should be screened as tests are easily available and not too costly. (2) Is there a TSH value above which we should terminate pregnancy? No recommendations from any of the scientific bodies advocating termination of pregnancy, no matter what the TSH level is.

Hyperthyroidism in pregnancy

Prevalence of thyrotoxicosis is rare (0.1- 1%). Most are Graves' disease (85%). 0.5 – 1% of pregnancies may have Gestational Thyrotoxicosis (GTT), a self - limiting disorder requiring no specific therapy. It should be remembered that 5 – 10% of normal subjects can have an undetectable TSH during the entire 9 months. MNG with toxicosis and autonomously secreting thyroid nodules are very rare and management is similar to Graves' disease (GD). The clinical manifestations of mild thyrotoxicosis can be difficult to distinguish from that of pregnancy and hence require laboratory tests: Elevated FT_3, FT_4, suppressed TSH with positive TRAb. The management will depend on when patient consults you for GD: before, during or after pregnancy:

Patient of GD planning pregnancy

A definitive treatment for GD should be advised; surgery (subtotal or total thyroidectomy) or Radio Active iodine ablation (RAIA). After RAIA, pregnancy should be planned only after six months for obvious reasons. The dose of RAI should be large enough so that thyrotoxicosis is controlled – a resulting hypothyroidism is acceptable in this situation. A definitive line of treatment is recommended because of adverse effects of antithyroid drugs (ATD) during pregnancy as all drugs cross placenta. The methimazole (MMI) and carbimazole (CBM) exposure causes congenital malformations such as aplasia cutis, choanal atresia and others. Propyl Thiouracil (PTU) had significantly lesser prevalence of embryopathy than MMI & CBM, hence given in first trimester; but it is associated with liver damage and hence not entirely safe.

First suspected to have GD in pregnancy

Graves' disease (GD) usually presents with severe symptoms of toxicosis and presence of goiter and positive TRAb, which is a very specific for GD. In GD, the accepted drug for management is PTU (100 – 200 mg three times daily) in the first trimester and MMI/CBZ after that. The smallest dose of required to keep FT_4 & FT_3 just above the normal nonpregnant range is ideal. Symptomatic treatment with beta-blockers (propranolol 20mg eight hourly) or atenolol 25 -50 mg/day can be given for 2 – 4 weeks, Too much of MMI/CBZ can produce hypothyroidism and goiter in the fetus and this needs to be avoided. Patient should be monitored with FT_4 and TSH 2 to 4 weekly in the initial period and when goals are achieved, once in 4 to 6 weeks. If remission occurs, drug should be discontinued. Thyroidectomy during pregnancy is rarely required and RAIA is contraindicated. There can be aggravation of GD after delivery as immune suppression of pregnancy disappears. Patients can safely continue ATD during lactation.

During pregnancy, the TRAb crosses placenta and this leads to transient neonatal toxicosis, fortunately this is very rare.

A close differential diagnosis of mild GD presenting first time in pregnancy is Gestational thyrotoxicosis (GTT) mediated by very high hCG levels. GTT is more common than GD in pregnancy; there is usually no goiter and the Thyroid receptor antibody (TRAb) is negative. The usual manifestation is exaggerated morning sickness causing dehydration with suppressed TSH. If severe, may require admission for IV fluids; this condition should not be treated with anti-thyroid drugs.

Patient on treatment for GD becomes pregnant

If well controlled for some time with CBM or MMI the antithyroid treatment is recommended to be changed to PTU (100 mg three times daily) in the first trimester and reinstitute methimazole or carbimazole in the second trimester by the ATA as in first suspected to have GD in pregnancy. FT4 should be maintained at higher normal range. There is a good chance of remission during the third trimester of pregnancy and hence when this is achieved, omit the antithyroid drug.

Other thyroid disorders

Goiter and Thyroid nodules discovered first time in pregnancy can await management till after delivery. Their evaluation is similar to non - pregnant women. In extremely rare cases, immediate management may be required and should be left to the specialists.

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