



## FOGSI MEDICAL DISORDERS IN PREGNANCY COMMITTEE

# Thyroid Update in Pregnancy



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January is 'Thyroid Awareness Month,' which calls for attention to the various health problems connected to the thyroid. While a lot of importance is given to other medical disorders in pregnancy, thyroid disorders are usually misdiagnosed and often not adequately treated. Therefore, this January 2021, FOGSI Medical Disorders in Pregnancy Committee has dedicated this newsletter to 'Thyroid Disorders in Pregnancy' – its symptoms, importance of diagnosis and treatment.

Pregnancy is delicate and it is necessary to be aware of the various factors that can prevent a healthy pregnancy. Awareness of such problems can lead to the prevention of complications. Thyroid awareness in pregnancy can prove to be a lifesaver for both mother and child.

Hope the articles gives you a complete overview of thyroid disorders in pregnancy.

Wishing you a Happy New Year.

Regards  
FOGSI Medical Disorders in Pregnancy Committee.



# HYPERTHYROIDISM IN PREGNANCY

**Dr. Kirtan M. Vyas**

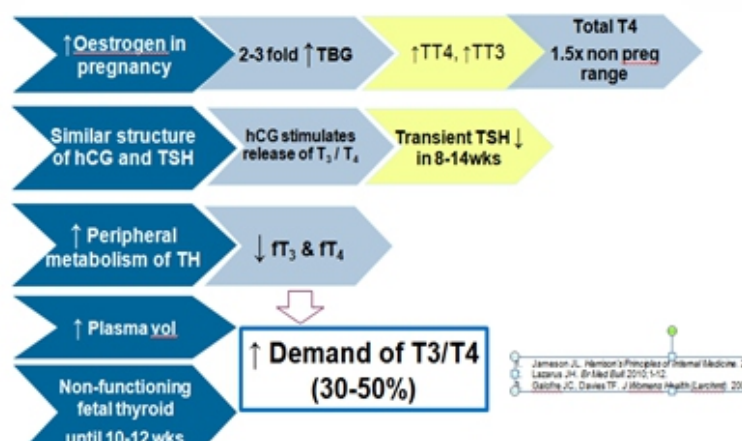
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- The pregnancy results in important physiological and hormonal changes that alter thyroid function mainly under the influence of  $\beta$ -HCG and estrogen.<sup>1</sup>

## Pregnancy is a Natural Stress Test for Thyroid Gland



- Overt hypothyroidism is increased in serum TSH (more than 10 mIU/L) as a result of decrease thyroxine and a negative feedback while subclinical hypothyroidism is serum TSH level in the range of 4-10 mIU/L with normal thyroxine ( $T_4$ ) levels.<sup>2,3</sup>

GUIDELINES	COUNTRY	TRIMESTER SPECIFIC RECOMMENDED TSH REF RANGE
ITS Guidelines 2012	India	<ul style="list-style-type: none"> <li>1<sup>st</sup> : 2.5 mIU/L</li> <li>2<sup>nd</sup> : 3.0mIU/L</li> <li>3<sup>rd</sup> : 3.0 mIU/L</li> </ul>
ETA Guidelines 2014	European	<ul style="list-style-type: none"> <li>1<sup>st</sup> : 2.5 mIU/L</li> <li>2<sup>nd</sup> : 3.0mIU/L</li> <li>3<sup>rd</sup> : 3.0 mIU/L</li> </ul>
ATA Guidelines 2017	American	<ul style="list-style-type: none"> <li>Use locally derived Reference ranges from a specified Pregnant population</li> <li>If the above is not available use and upper TSH reference limit of 4.0 mIU/L</li> </ul>

- Maternal hypothyroidism in pregnancy is due to autoimmunity post-thyroidectomy or iodine deficiency (Hashimotos thyroiditis is the commonest cause in pregnancy). The incidence of overt hypothyroidism is 0.2-2.5 % and that of subclinical hypothyroidism is 2-7%. Infact thyroid antibodies are present in almost 60% of reproductive age women.<sup>4</sup>
- Hypothyroidism is responsible for so many adverse pregnancy outcomes.<sup>5</sup>

**EFFECTS OF HYPOTHYROIDISM IN PREGNANCY**

MATERNAL	FOETAL	NEONATAL
Anaemia and CHF	Cognitive impairment	Hyperbilirubinemia
Pre-eclampsia	Neurological abnormalities	Respiratory distress
Placental abnormalities	Developmental abnormalities	
Low Birth Weight infants	Congenital Hypothyroidism	
Post partum hemorrhage		
Myopathy		

- Pregnancies in women with subclinical hypothyroidism were 3 times more likely to be complicated by placental abruption. Preterm birth was almost 2-fold higher in women with subclinical hypothyroidism.<sup>6</sup>

**ITS & FOGSI 2019 RECOMMENDATIONS FOR THE MANAGEMENT OF THYROID DYSFUNCTION IN PREGNANCY****MANAGEMENT OF OVERT HYPOTHYROIDISM**

During Pregnancy, all patients with overt hypothyroidism with TSH > 2.5 mIU/L should be treated with Levothyroxine (LT4) dose 1.6-2.0 µg/kg/day. Maintain the target TSH levels ≤2.5 mIU/L. In patients with pre-existing hypothyroidism, Levothyroxine(LT4) dose increased by 30% as soon as pregnancy is diagnosed. Regular TSH monitoring (approximately every 4-6 weeks until mid-gestation and at least once near 28 weeks gestation) should be done.

**MANAGEMENT OF SUBCLINICAL HYPOTHYROIDISM IN PREGNANCY**

LT4 therapy is recommended for women with a TSH greater than 10.0 mIU/L and TPOAb positive women with a TSH between 4 mIU/L and 10.0 mIU/L. LT4 therapy can be considered for women with TPOAb negative with a TSH between 4 mIU/L and 10.0 mIU/L and TPOAb positive women with a TSH between 2.5 mIU/L and 4 mIU/L.

**MANAGEMENT OF HYPOTHYROIDISM POST-PARTUM**

Post-delivery the patient should be reverted back to the prepregnant dosage and TSH levels should be rechecked after 6 weeks. Some women in whom LT4 is initiated during pregnancy may not require LT4 postpartum. Such women are candidates for discontinuing LT4, especially when the LT4 dose is ≤50 mcg daily. If LT4 is discontinued, serum TSH should be evaluated in ~ 6 weeks. Women with thyroid autoimmunity need annual monitoring with TSH.

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# HYPOTHYROIDISM IN PREGNANCY

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## Introduction:

Thyroid disorders are commonly encountered during pregnancy. Hyperthyroidism however is seen in less than 1 % of pregnant females in India.

Hyperthyroidism can be defined as 'Increased thyroid hormone production due to an overactive thyroid gland'.

The hormones namely T3 and T4 circulate in the body bound to – Thyroxine binding globulin (TBG), transthyretin and albumin. T4 is the one found in majority among the released hormones. The active form is also the unbound version found in very small quantities and is labeled as free T4. Another important hormone is 'Thyroid stimulating hormone' (TSH) which is released from the anterior pituitary and it regulates the production of thyroid hormones.

## Physiological changes of thyroid hormones in pregnancy:

During pregnancy, there are a lot of alternations noted in the thyroid hormone levels.

Tests	Normal Pregnancy	Hyperthyroidism
Thyroid Stimulating Hormone (TSH)	Normal or no change	Decreased
T3	Increased	Increased or normal range
FT3	Normal range	Increased or normal range
T4	Increased	Increased
FT4	Normal range	Increased

Human chorionic gonadotropin (HCG) interacts and stimulates the TSH receptors in the thyroid gland thus mimicking an effect of hyperthyroidism. During the first trimester of pregnancy, Rising levels of HCG are noted which result in low or suppressed TSH values and a mild transient increase in the levels of T4. Hence a continuous monitoring is indicated as the TSH values would further fall back to their normal range in the second or third trimester due to decrease in the HCG levels.





Thyroid hormones have an important role during the early development of the fetus and also for the continuation of the pregnancy. Untreated thyroid disorders may cause complications during pregnancy and make the fetus susceptible to developmental disorders both short term as well as long term.

### Causes of Hyperthyroidism in pregnancy:

Thyrotoxicosis (a clinical condition due to increased levels of circulating thyroid hormones) in pregnancy may be due to multiple causes:

- Intrinsic disease of the thyroid:
  1. Graves' disease
  2. Thyroid nodule
  3. Sub-acute thyroiditis
- Pregnancy Induced:
  1. Hyperemesis
  2. Hydatidiform mole
- Miscellaneous:
  1. Drug induced

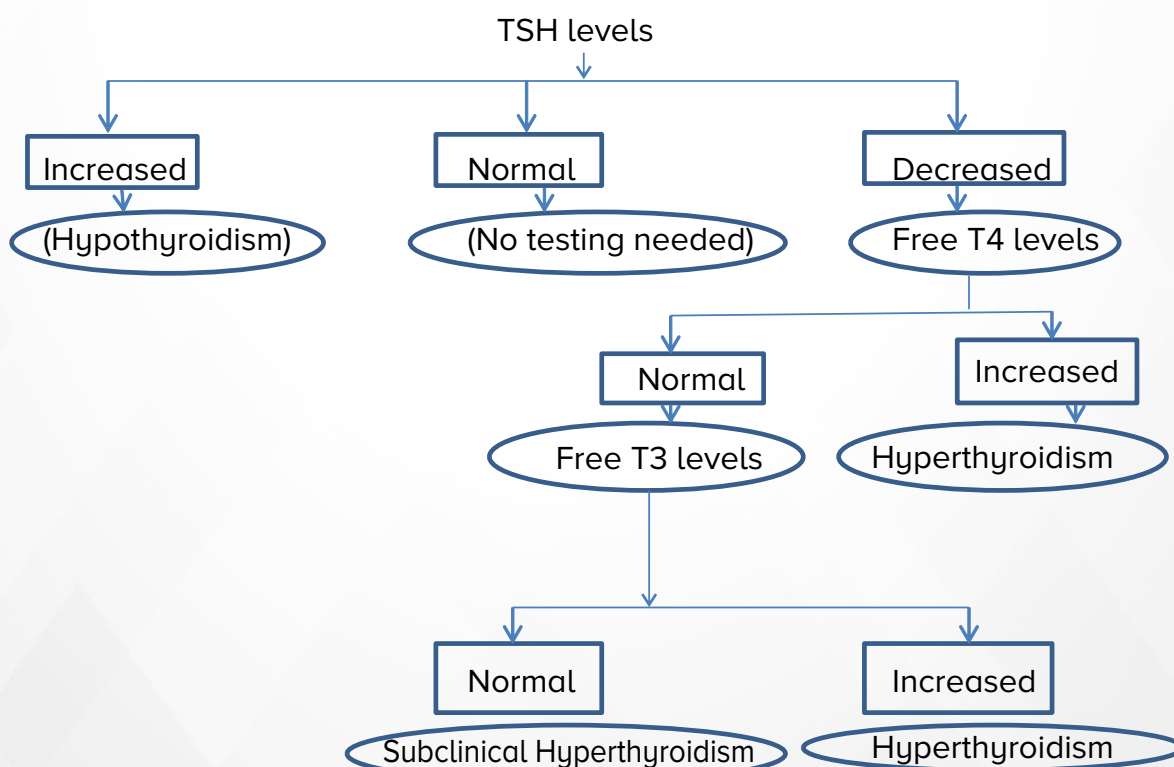
Graves' disease is one of the common causes of a pre-existing hyperthyroidism which is autoimmune in nature and seen in women. Thyroid stimulating hormone receptor antibody (TSH RAb) is the reason for the stimulation of the thyroid gland resulting in Graves' disease.

### Diagnosis of Hyperthyroidism in pregnancy:

Symptoms: Sweating, palpitations, heat intolerance, weight loss or failure to gain weight, nausea etc.

Signs: Tremors, warm extremities, tachycardia, proptosis, goiter etc. Another sign commonly seen in hyperthyroidism on the ECG is atrial fibrillation.

### Algorithm for Thyroid Testing:



**Fetal effects of maternal Hyperthyroidism:**

The embryogenesis of the thyroid gland is generally complete and it begins the production of thyroid hormones by the 12<sup>th</sup> week of gestation. So, the fetus is totally dependent on the maternal thyroid hormones within the first 12 weeks of pregnancy. In cases of uncontrolled hyperthyroidism in pregnancy, there may be presence of intrauterine growth retardation, fetal tachycardia and goiter formation in the fetus.

Documentation of fetal heart sounds for fetal tachycardia along with fetal thyroid size for fetal goiter should be done on obstetric scans (anomaly scans and subsequent growth scans).

**Management:**

The management of hyperthyroidism in pregnancy includes anti-thyroid drugs (ATD). Radioactive iodine is contraindicated in pregnancy.

ATDs belong to the class of thioamides which act by blocking the production of thyroid hormones in the thyroid gland. The drugs generally used are Propylthiouracil (PTU) and Methimazole. The aim of ATD therapy is to attempt to maintain the range of thyroid hormones at its upper point of the normal range with the minimum possible dosages of the drugs.

All the ATDs cross the placental barrier and so they may cause a risk of birth defects during the initial phases of pregnancy and may also have a potential risk of causing hypothyroidism in the fetus during the last trimester of pregnancy.

It is recommended to initiate therapy with PTU during the first trimester and later shift over to Methimazole during second trimester of pregnancy. Liver function tests have to be monitored due to potential risks of liver failure seen in patients on treatment of hyperthyroidism with PTU.

**Drug Dosages:****1. Propylthiouracil (PTU):****a) Hyperthyroidism:**

Initial dose:-300 -450 mg/day to be administered orally in 3 divided doses.  
Maintenance dose:-100 -150 mg/day to be administered orally in 3 divided doses.

**a) Graves' disease in Pregnancy:**

Initial dose:-50 – 150 mg to be administered orally three times a day.  
Maintenance dose:-50 mg to be administered orally twice or three times a day.



## **1. Methimazole:**

### **a) Hyperthyroidism**

Initial dose: 15 - 40 mg/day to be administered orally in divided doses in mild and moderate cases. Dosages of 60mg/day can be used in severe cases.

Maintenance dose: 5 – 30 mg/day to be administered orally in three divided doses.

### **b) Graves' disease in pregnancy**

Initial dose: 10 – 20 mg/day to be administered orally once a day.

Maintenance dose: to be changed as per the reduction in thyroid function tests

The titration of the drug dosages have to be done based on the FT4 levels and not the TSH as the TSH values take multiple weeks to return back to its reference range.

The ATD dosages have to be reduced when the FT4 levels reach the upper limit of the normal range.

### **Thyroid function tests and its monitoring:**

Thyroid function tests should be checked once in every 3 to 4 weeks at the time of starting the treatment. The dose adjustments of the drugs should be done on the FT4 values as the TSH normalization is delayed during the first few months.

### **Side effects/ Complications of the ATDs:**

Simple: Rash, fever, urticarial.

Severe: Hepatitis or liver toxicity, SLE like syndrome, agranulocytosis.

### **Management in postpartum patients of hyperthyroidism:**

Relapse of Graves' disease is seen in a large number of females within 3 months of their delivery. This may be due to the disappearance of Immunosuppression of pregnancy. TSH and FT4 values need to be monitored at 6 weeks and 12 week interval.

PTU and methimazole both are generally excreted in breast milk. PTU is about 80% protein bound whereas methimazole is non-protein bound and more lipid soluble.

### **References:**

1. De Swiet's Medical disorders in Obstretic Practice, 5<sup>th</sup> edition.
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## POSTPARTUM THYROIDITIS

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Postpartum thyroiditis is a destructive thyroiditis induced by an autoimmune mechanism within one year after parturition. Postpartum thyroiditis, like painless thyroiditis, is considered a variant form of chronic autoimmune thyroiditis (Hashimoto's thyroiditis)

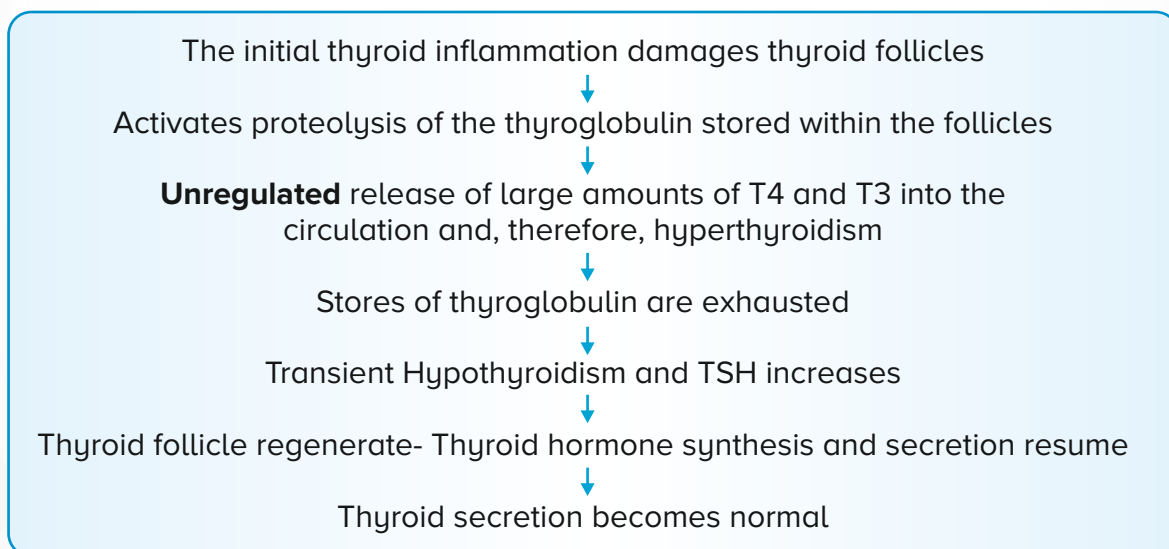
The reported prevalence of postpartum thyroiditis varies globally and ranges from 1 to 17 percent. It occurs more often in women with a previous history of postpartum thyroiditis, positive antithyroid peroxidase antibody titers, and type 1 diabetes.

Presentation: It may present in one of the 3 ways:

1. Transient hyperthyroidism alone
2. Transient hypothyroidism alone
3. Transient hyperthyroidism followed by hypothyroidism and then recovery

Most women recover and are euthyroid within one year postpartum. However, some women never recover from the initial hypothyroid phase and have permanent hypothyroidism or goitre.

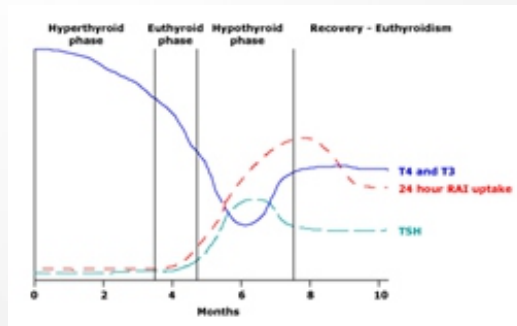
Characteristic course of thyroiditis (painless, postpartum, or subacute)



### Clinical Manifestations:

Clinical manifestation of postpartum thyroiditis can be variable

**Approximately 20 to 30 percent** of women with postpartum thyroiditis have the characteristic sequence of hyperthyroidism, which usually begins one to four months after delivery and lasts two to eight weeks, followed by hypothyroidism, which lasts from approximately two weeks to six months, and then recovery







**20 to 40 percent** have only hyperthyroidism which begins two to six months after delivery. Symptoms are typically mild and consist mainly of fatigue, weight loss, palpitations, heat intolerance, anxiety, irritability, tachycardia, and tremor.

Remaining **40 to 50 percent** have only hypothyroidism, which begins two to six months after delivery. Symptoms are usually mild, leading to lack of energy, cold intolerance, constipation, sluggishness, and dry skin.  
Some women do not restore normal endogenous thyroid function after the initial episode of hypothyroidism.

Most women with postpartum thyroiditis have a mildly enlarged, diffuse, nontender thyroid gland when their thyroid function is abnormal, which disappears with recovery. In some women, however, goitre is the presenting complaint.  
Postpartum hypothyroidism may decrease milk volume.

### Laboratory findings:

Thyroid function test evaluation includes free T3, free T4 and TSH.

Hyperthyroid phase	High or normal free T4 and T3	Low TSH
Hypothyroid phase	Low or normal Free T4 and T3	High TSH

Anti-thyroid antiperoxidase antibodies concentrations are high in 60 to 85 percent of women with postpartum thyroiditis and are highest during the hypothyroid phase or soon thereafter. Routine laboratory studies are usually normal, but some women have a slightly increased erythrocyte sedimentation rate and/or C-reactive protein.

Thyroid aspirations are not typically required unless there is a specific indication, such as detection of a thyroid nodule. If FNAC done the HPE may show lymphocytic infiltration with collapsed follicles. Radioiodine uptake and scanning is not usually necessary and is contraindicated during breast feeding.

### Diagnosis:

High degree of clinical suspicion based on the presenting features and backed up by laboratory test of thyroid functions form a base for diagnosis.

Women with hypothyroidism also are prone to postpartum depression (PPD). It is therefore prudent to investigate women presenting with PPD for thyroid disorders.

### Differential diagnosis:

Hyperthyroid phase should be differentiated with Grave's disease:

	Postpartum thyroiditis	Grave's disease
Onset	Within 3 months of delivery	More than 6 months post delivery
Clinical features	Mild symptoms, no significant thyroid enlargement, no ophthalmopathy	More symptomatic, thyroid enlargement, ophthalmopathy present
Laboratory findings	Free T4 > Free T3	Free T3 > Free T4
Thyrotropin receptor antibody	Not elevated	Elevated

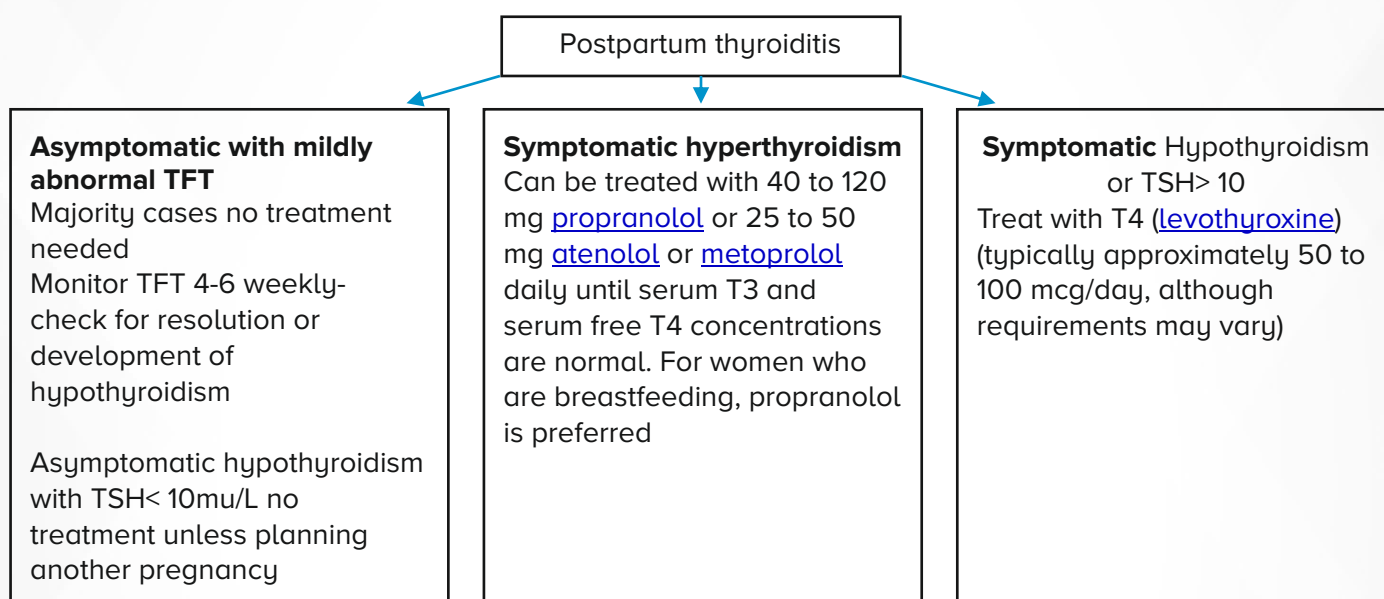


The hypothyroid phase of postpartum thyroiditis must be differentiated from lymphocytic hypophysitis, which also may occur during late pregnancy or the postpartum period. In lymphocytic hypophysitis, the serum TSH is expected to be inappropriately normal or low in the context of a low free T4, whereas in hypothyroidism with postpartum thyroiditis, the TSH should be elevated in conjunction with a decreased free T4.

Screening:

Routine screening for Postpartum thyroiditis is not recommended. However, women at highest risk for developing postpartum thyroiditis (eg, antithyroid peroxidase antibody positive, type 1 diabetes, previous episode of postpartum thyroiditis) should have a serum TSH measurement at three and six months postpartum. If the TSH level is abnormal, it should be repeated soon thereafter along with a free T4 level and T3, within one to two weeks.

**Management:** Approach as per endocrine society and American thyroid association (ATA)



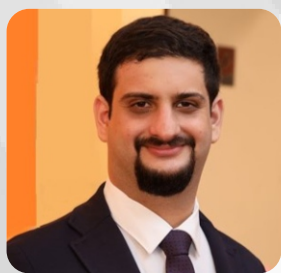
#### Duration of treatment:

Since Postpartum thyroiditis is often transient, the levothyroxine dose can be weaned after 6-12 months, unless the woman is pregnant, planning pregnancy or still breast feeding. It is advisable to assess TSH and free T4 6 weeks after stopping. Up to 30 percent of women never recover from the initial hypothyroid phase, and a rising TSH level during drug weaning is indicative of persistent hypothyroidism, requiring long term levothyroxine. For women who have fully recovered from postpartum thyroiditis, it is recommended to measure serum TSH levels annually, particularly within 5 to 10 years after the initial diagnosis.

Any woman who has had postpartum thyroiditis should be told that recurrence is likely after future pregnancies and that she is at substantial risk for the later development of hypothyroidism or goitre.

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# THYROID AND PREGNANCY: MYTHS AND REALITIES.

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## **Myth 1: Pregnancy is not possible in women with hypothyroidism**

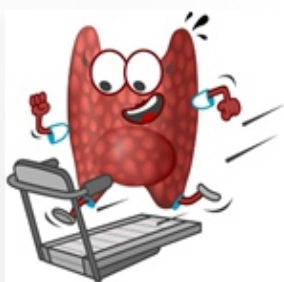
**Reality:** Subclinical hypothyroidism may be associated with ovulatory dysfunction. However it is possible to get pregnant with hypothyroidism with recognition, diagnosis, monitoring and treatment. Neglecting the condition could lead to difficulty in conception and complications during pregnancy.

## **Myth 2: If TSH levels in pregnancy are in normal ranges as per laboratory values then there is no need for treatment.**

**Reality:** Laboratories report TSH values of 0.5 to 5.0 mIU/L as normal for women. However values in pregnancy vary in each trimester. The trimester specific ranges for TSH are 0.6–3.4 mIU/L in the first trimester, 0.37–3.6 mIU/L in the second trimester and 0.38–4.0 mIU/L in the third trimester. Measurement of free T3 and T4 and TPO antibodies are useful in clinching the diagnosis and are recommended if TSH levels exceed 2.5 mIU/L.

## **Myth 3: Thyroid medication has to be stopped during pregnancy**

**Reality:** It is essential to continue thyroid medication during pregnancy to maintain optimum control and safe obstetric outcomes. The doses need to be adjusted by periodic testing to avoid undertreatment or overcorrection. Treatment is now recommended if TSH levels are >2.5 mIU/L and TPO antibodies test positive.



## **Myth 4: Elevated thyroid antibodies cause increased fetal loss and impacts neonatal health**

**Reality:** An increase in fetal loss, preterm delivery, perinatal mortality and LGA infants is reported in euthyroid women with elevated TPO antibodies. It is however not clear if TPO antibodies affect cognitive development. Euthyroid women with elevated TPO antibodies are at high risk of developing hypothyroidism and in them TSH should be measured every 4 weeks in the first trimester and if stable once each in the second and third trimesters.

## **Myth 5: Hyperemesis gravidarum causes hyperthyroidism during pregnancy**

**Reality:** The high levels of hCG seen in hyperemesis gravidarum may cause measurable, transient hyperthyroidism in early pregnancy, since hCG itself has a weak thyroid-stimulating activity.

Definitive diagnosis of thyroid disease is based on a careful review of history, physical exam and laboratory testing and judicious observation before initiating treatment.

**Myth 6: Hypothyroidism can be responsible for excessive weight gain during pregnancy**

**Reality:** Although the thyroid gland is responsible for metabolism it is extremely rare for patients to experience significant weight gain if they have an untreated hypothyroidism. In severe hypothyroidism there could be weight gain due to fluid retention and it is this weight which is lost with thyroid hormone replacement.



**Myth 7: Excess Iodine is required during pregnancy to maintain normal thyroid function**

**Reality:** Iodine requirements are higher in pregnant women due to an increase in maternal T4 production. Iodine deficiency is associated with hypothyroidism and goitre. The diet should have approximately 250 micrograms as a daily intake. This requirement continues during lactation. However excess iodine from seaweed supplements could be harmful.

**Myth 8: Soy based products are detrimental to thyroid disorder**

**Reality:** Soy based products can decrease absorption of thyroid medication. Medication should be had first thing in the day on an empty stomach but never in the same meal as soy.

**Myth 9: A gluten free diet can help Hashimoto's thyroiditis in pregnancy**

**Reality:** Hashimoto's thyroiditis is the most common cause of hypothyroidism. A gluten free diet cannot reverse Hashimoto's. This myth has probably arisen because coeliac disease is common in with 'Hashimotos disease and coeliac disease benefits from excluding gluten from diet.

**Myth 10: Thyroid medication is secreted in breast milk and could affect the neonate**

**Reality:** Only a small amount of thyroid hormone reaches the neonate through breast milk. The treatment must be continued with lactation and adjusted according to TSH levels assessed during puerperium.