
بسم الله الرحمن الرحيم
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Thyroid in Pregnancy

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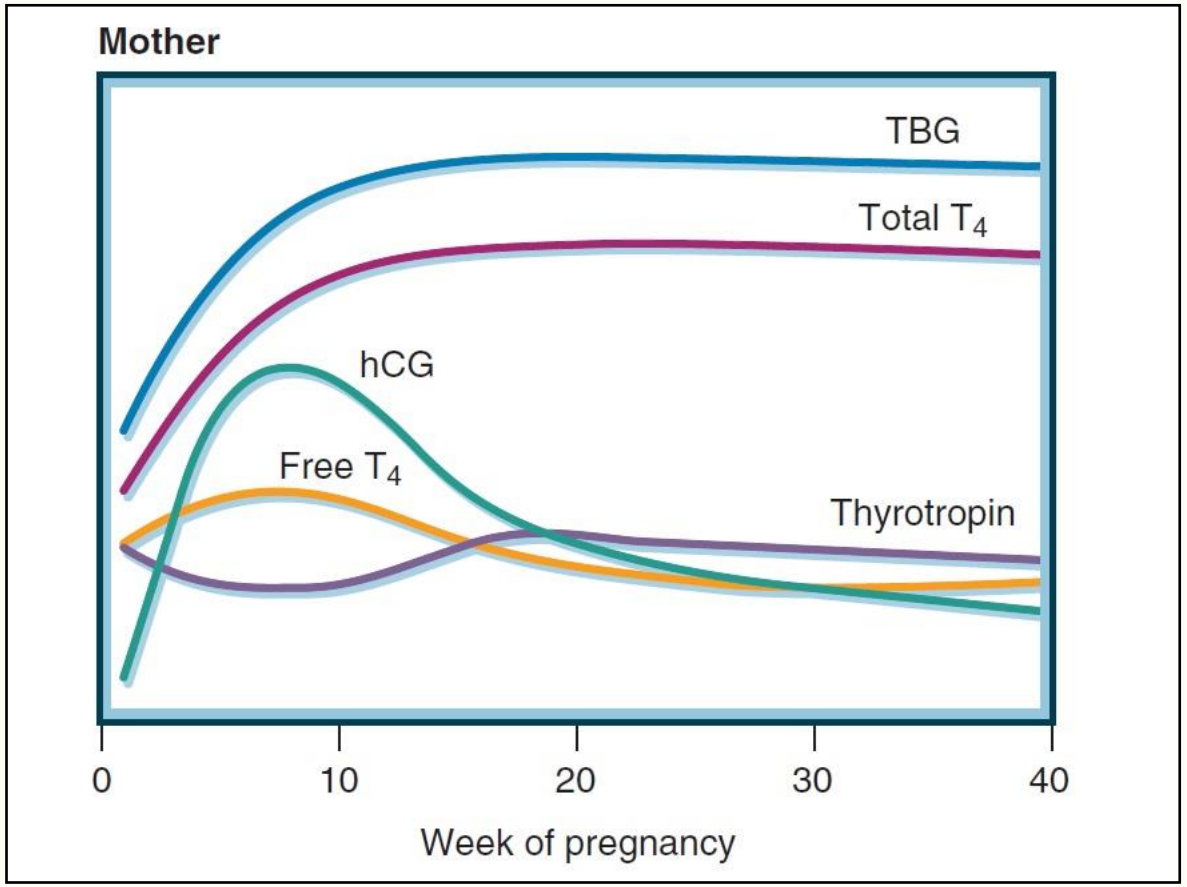
How do thyroid function tests change during pregnancy?



What is the normal reference range for serum TSH concentrations in each trimester of pregnancy?

- A downward shift of the TSH reference range occurs during pregnancy, with a reduction in both the **lower** (decreased by about 0.1–0.2 mU/L) and the **upper limit** of maternal TSH (decreased by about 0.5–1.0 mU/L), relative to the typical nonpregnant TSH reference range.

- Initial studies of pregnant women in the United States and Europe first led to recommendations for a TSH **upper** reference limit of **2.5 mU/L** in the **first trimester** and **3.0 mU/L** in the **second** and **third trimesters**.

IODINE STATUS AND NUTRITION

Dietary iodine requirements are **higher in pregnancy** than they are for nonpregnant adults, because of:

- increased thyroid hormone production
- increased renal iodine excretion
- increased fetal iodine requirements

Groups of pregnant women whose **median UICs** are:

- 50–150 µg /L are defined as mildly to moderately iodine deficient.
- <50 µg /L are defined as severe iodine deficient.

IODINE STATUS AND NUTRITION

Median UICs can be used to assess the iodine status of **populations**, but single spot or 24-hour UICs are not a valid marker for the iodine nutritional status of **individual** patients, Because there is substantial diurnal and day-to-day variation in urinary iodine excretion.

What is the impact of iodine deficiency on the **mother**, **fetus**, and **child**?

Maternal dietary iodine deficiency results in impaired **maternal** and **fetal** thyroid hormone synthesis.

Low thyroid hormone values stimulate

- increased pituitary TSH production
- increased TSH stimulates thyroid growth, resulting in maternal and fetal **goiter**

What is the impact of iodine deficiency on the **mother**, **fetus**, and **child**?

Severe iodine deficiency in pregnant women has been associated with:

- increased rates of **pregnancy loss**, **stillbirth**
- increased **perinatal** and **infant mortality**

Mild to moderate iodine deficiency in pregnant women has been associated with:

- reduced **neonatal head circumference**
- attention deficit and hyperactivity disorders (**ADHD**) in children
- impaired **cognitive** outcomes

What is the recommended daily iodine intake in women **planning pregnancy**, women who are **pregnant**?

All pregnant women should ingest approximately **250 µg** iodine daily.

Women who are **planning pregnancy** or **currently pregnant**, should supplement their diet with a daily oral **supplement** that contains **150 µg** of iodine in the form of potassium iodide.

There is no need to initiate iodine supplementation in pregnant women who are being treated for **hyper**thyroidism or who are taking **LT4**.

What is the recommended daily iodine intake in women **planning pregnancy**, women who are **pregnant**?

Excessive doses of iodine exposure during pregnancy should be avoided.

Sustained iodine intake from diet and dietary supplements **exceeding 500 µg** daily should be avoided during pregnancy due to concerns about the **potential for fetal thyroid dysfunction.**

THYROID AUTO-ANTIBODIES AND PREGNANCY COMPLICATIONS

Anti-TPO or anti-Tg thyroid autoantibodies are present in 2% to 17% of pregnant women.

In women with **thyroid autoimmunity**, **hypothyroidism** may occur because of the **stress of pregnancy**.

TPO antibodies are able to **cross the placenta**. However, maternal passage of either TPO-Ab or Tg-Ab is not associated with fetal thyroid dysfunction.

Euthyroid pregnant women who are TPO-Ab or Tg-Ab positive should have measurement of serum TSH concentration performed **at time of pregnancy confirmation** and **every 4 weeks** through midpregnancy.

THE IMPACT OF THYROID ILLNESS UPON INFERTILITY

Overt thyroid dysfunction

- Irregular menses may occur
- increased risk of infertility
- LT4 treatment is recommended

Subclinical hypothyroidism

- Insufficient evidence exist to determine if LT4 therapy improves fertility in **subclinically hypothyroid**, Anti-Tpo–negative women

Anti-Tpo positive **euthyroid** women

- no recommendation for LT4 therapy

HYPOTHYROIDISM AND PREGNANCY

Overt thyroid dysfunction

When available, population- and trimester-specific reference ranges for serum TSH during pregnancy should be defined.

Reference ranges should be defined in healthy TPOAb-negative pregnant women with optimal iodine intake and without thyroid illness.

If pregnancy-specific TSH reference ranges are not available, an upper reference limit of 4.0 mU/L may be used.

HYPOTHYROIDISM AND PREGNANCY

What **adverse outcomes** are associated with overt hypothyroidism during pregnancy?

Effects upon fetal neurocognitive development

increased risks of:

- premature birth
- low birth weight
- pregnancy loss
- lower offspring IQ

HYPOTHYROIDISM AND PREGNANCY

What **adverse outcomes** are associated with subclinical hypothyroidism during pregnancy?

These include:

- adverse effects on pregnancy outcome (i.e., pregnancy loss)
- adverse perinatal outcomes (i.e., premature delivery, hypertensive disorders)
- Adverse neurocognitive outcomes (IQ) in offspring

LT4 therapy

is recommended for:

- TPOAb-negative women with a TSH >10.0 mU/L
- TPOAb-positive women with a TSH >4.0 mU/L

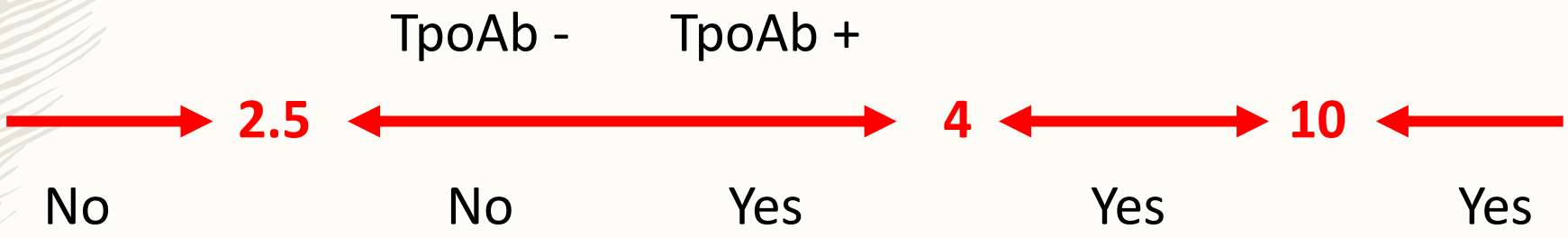
may be considered for:

- TPOAb-negative women with 4.0 mU/L <TSH <10.0mU/L
- TPOAb-positive women with 2.5 mU/L <TSH <4.0 mU/L

not recommended for:

- TPOAb-negative women with a normal TSH (TSH <4.0 mU/L)

LT4 therapy



LT4 therapy

Target of TSH → lower half of the trimester-specific reference range (**<2.5** mu/l)

Monitore with TSH → approximately **every 4 weeks** **until midgestation** and **at least once near 30** weeks gestation.

Preconception LT4 adjustment in treated hypothyroid women (receiving LT4) planning pregnancy?

serum TSH should be evaluated preconception, and LT4 dose adjusted to achieve a TSH value between 0.5 and 2.5 mU/L.

Hypothyroid patients receiving LT4 treatment with a **suspected or confirmed pregnancy** should increase their dose of LT4 by 20%–30%.

Postpartum LT4 adjustment

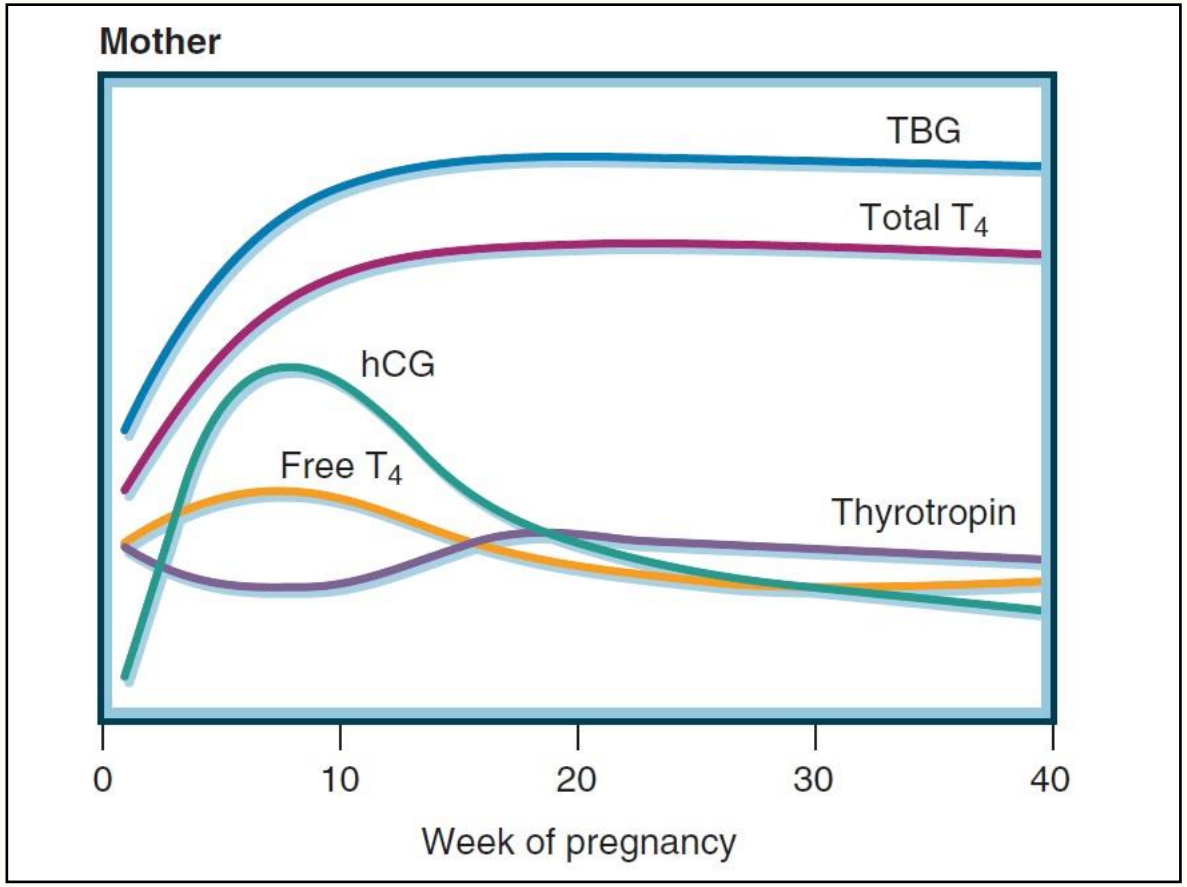
Following **delivery**, LT4 should be reduced to the patient's preconception dose. Additional thyroid function testing should be performed at approximately 6 weeks post partum.

Some women in whom LT4 is **initiated during pregnancy** may not require LT4 post partum. Such women are candidates for discontinuing LT4, especially when the LT4 dose is ≤50 µg/d.

If LT4 is discontinued, serum TSH should be evaluated in approximately 6 weeks.

THYROTOXICOSIS IN PREGNANCY

A **peak hCG** level typically occurs between 7 and 11 weeks gestation



THYROTOXICOSIS IN PREGNANCY

Gestational transient thyrotoxicosis

It is limited to the **first half** of pregnancy

↑**FT4** and suppressed **TSH**

secondary to elevated **hCG** (hyperemesis gravidarum)

hCG-induced thyrotoxicosis (multiple gestation, hydatidiform mole and choriocarcinoma)

management of hyperemesis gravidarum includes:

Supportive therapy, management of dehydration, and hospitalization if needed.

ATDs are not recommended, though b-blockers may be considered

THYROTOXICOSIS IN PREGNANCY

Graves' Disease

What is the management of patients with GD **during pregnancy**?

Poor control of thyrotoxicosis is associated with:

- pregnancy loss
- pregnancy induced hypertension
- Prematurity
- low birth weight
- intrauterine growth restriction
- Stillbirth
- thyroid storm, and maternal congestive heart failure

THYROTOXICOSIS IN PREGNANCY

Graves' Disease

Methimazole and PTU adverse effect:

- allergic reactions
- Agranulocytosis
- hepatotoxicity (PTU)

PTU limited use for:

- first trimester of pregnancy
- MMI allergy
- Thyroid storm

THYROTOXICOSIS IN PREGNANCY

Graves' Disease

Methimazole teratogenic effects (during gestational weeks 6–10):

aplasia cutis

syndrome of **methimazole embryopathy** was described, which also includes dysmorphic facies

choanal or **esophageal atresia**

Umbilicocele

eye, **urinary system**, and **ventricular septal defects**

PTU birth defects

face and neck cysts

urinary tract abnormalities (in males)

THYROTOXICOSIS IN PREGNANCY

Graves' Disease

In a **newly pregnant** woman with **GD**, who is euthyroid on a low dose of MMI (≤5–10 mg/d) or PTU (≤100– 200 mg/d), the physician should consider discontinuing all antithyroid medication.

The risk of rapid relapse of hyperthyroidism after medication withdrawal in early pregnancy is high in patients:

- who have been treated for a short period (<6 months)
- who have suppressed or low serum TSH while on medication prepregnancy
- who require >5–10mg of MMI per day to stay euthyroid
- who have active orbitopathy or large goiter
- who have high levels of TRAb

THYROTOXICOSIS IN PREGNANCY

Graves' Disease

In pregnant women with a high risk of developing thyrotoxicosis if antithyroid drugs were to be discontinued:

PTU is recommended for the treatment of maternal hyperthyroidism through 16 weeks of pregnancy. Pregnant women receiving MMI who are in need of continuing therapy during pregnancy should be switched to PTU as early as possible.

When shifting from MMI to PTU, a dose ratio of approximately 1:20 should be used.
If ATD therapy is required **after 16 weeks** gestation, it remains unclear whether PTU should be continued or therapy changed to MMI.

Antithyroid medication during pregnancy should be administered at the **lowest effective dose** of MMI or PTU, **targeting** maternal serum TT4 at the **upper limit or moderately above** the reference range

THYROTOXICOSIS IN PREGNANCY

Graves' Disease

Thyroidectomy should be considered:

- in cases of **allergies/contraindications** to both ATDs
- in the patient who is **not compliant** with drug therapy
- in women in whom **euthyroidism cannot be achieved** even on large doses of ATDs

If surgery is indicated, the **second trimester** is the optimal time.

Thyroidectomy is often followed by a gradual, but not immediate disappearance of **TRAb**, and withdrawal of ATD in the mother after thyroidectomy may lead to **isolated fetal hyperthyroidism.**

If maternal **TRAb** concentration is high (>3 times the ULN) the fetus should be carefully monitored for development of fetal hyperthyroidism throughout pregnancy, even if the mother is euthyroid post thyroidectomy.

THYROTOXICOSIS IN PREGNANCY

Graves' Disease

Fetal risks in women with previous or current GD:

poor control of hyperthyroidism throughout pregnancy may induce transient central hypothyroidism

excessive amounts of ATDs may be responsible for fetal and neonatal hypothyroidism

high levels of TRAb in the second half of pregnancy may induce fetal and neonatal hyperthyroidism

How is neonatal hypo or hyperthyroidism treated?

All newborns should be screened for hypothyroidism by blood spot analysis typically 2–5 days after birth.

Neonatal hypothyroidism

In women receiving ATDs at the time of delivery

return of normal thyroid function, typically within 3–5 days

Neonatal hyperthyroidism (transfer of TRAb to the fetus):

Typically, **neonatal GD** does not present until the end of the first week of life when **maternal ATD, but not the TRAb, have been cleared** from the neonatal circulation.

The usual duration of neonatal GD is 1–3 months.

Treatment → MMI (0.5–1 mg/d), Propranolol (2 mg/kg)

screening for THYROID DYSFUNCTION before or during PREGNANCY

All patients **seeking pregnancy**, or **newly pregnant**, should undergo clinical evaluation, If any of the following risk factors are identified:

1) A **history of** hypothyroidism/hyperthyroidism or current symptoms/signs of thyroid dysfunction
2) Known TPO-Ab positivity or presence of a goiter
3) History of head or neck radiation or prior thyroid surgery
4) Age >30 years
5) Type 1 diabetes or other autoimmune disorders
6) **History of** pregnancy loss, preterm delivery, or infertility
7) Multiple prior pregnancies (≥2)
8) Family history of autoimmune thyroid disease or thyroid dysfunction
9) Morbid obesity (BMI ≥40 kg/m2)
10) Use of amiodarone or lithium, or recent administration of iodinated radiologic contrast
11) Residing in an area of known moderate to severe iodine insufficiency

POSTPARTUM THYROIDITIS

an **inflammatory autoimmune** condition

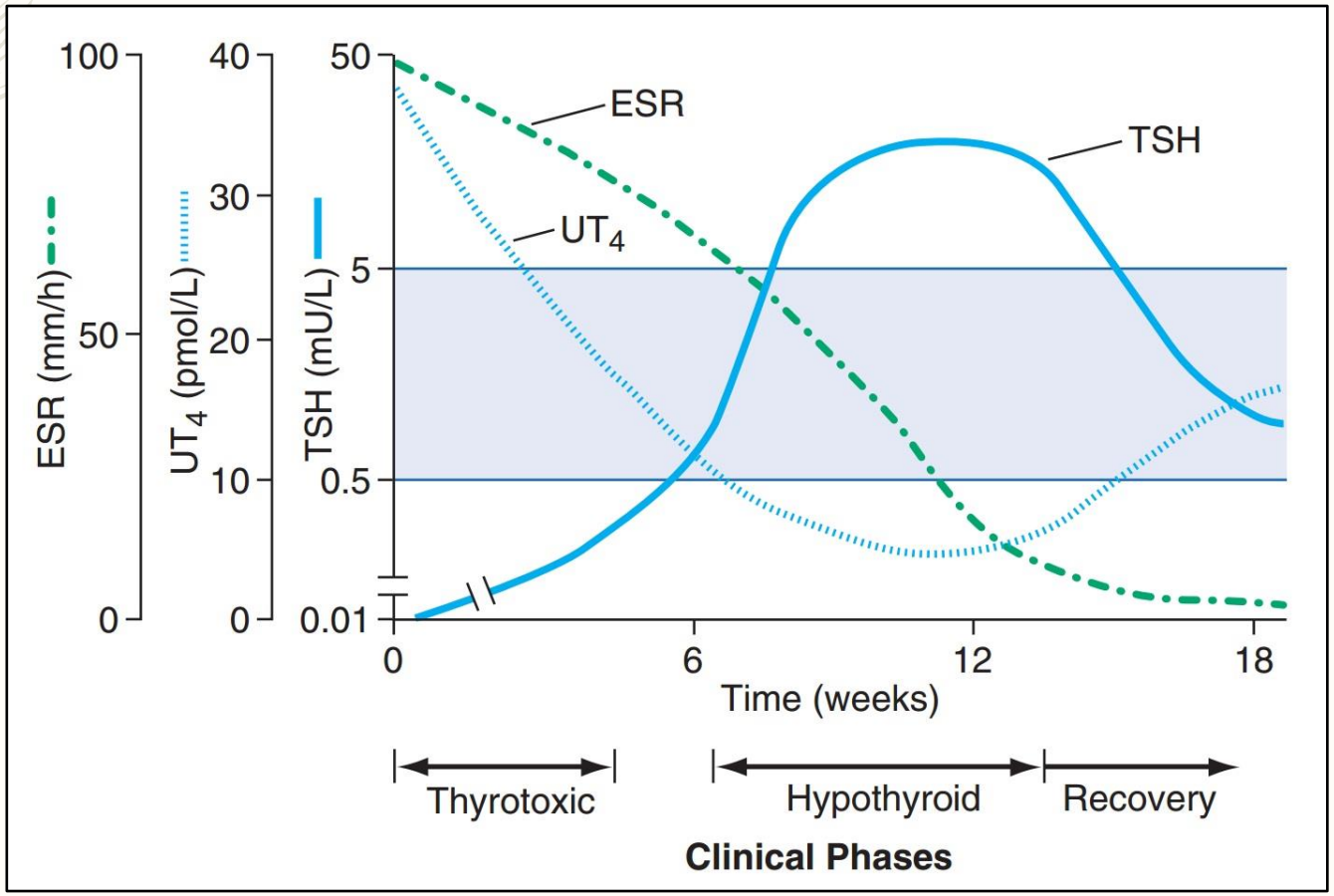
in **first** postpartum **year**

in women who were **euthyroid prior to pregnancy**

In the classic form:

- transient **thyrotoxicosis** (between 2 and 6 months post partum)
- Is followed by transient **hypothyroidism** (from 3 to 12 months postpartum)
- with a return to the **euthyroid** state by the end of the initial postpartum year (10%–20% of cases resulting in permanent hypothyroidism)

POSTPARTUM THYROIDITIS



POSTPARTUM THYROIDITIS

Women who are thyroid Ab positive (TPOAb and TgAb) in the **first trimester** have a high risk of developing PPT, ranging from 33% to 50%.

Women with the highest Ab titers also have the highest risk of PPT.

The occurrence of PPT reflects the **rebound** of the immune system in the postpartum period after the relative immune suppression of pregnancy.

Painless condition and most women are **asymptomatic** or only mildly symptomatic during the **thyrotoxic phase**.

The **hypothyroid phase** of PPT is **more frequently symptomatic**.

POSTPARTUM THYROIDITIS

differentiation from thyrotoxicosis caused by GD:

TRAb is positive in GD and is typically negative in PPT

An elevated **T4:T3 ratio** suggests the presence of PPT

Physical stigmata of GD, such as **goiter** with a **bruit** or **ophthalmopathy**

The **radioiodine uptake** is elevated or normal in GD and low in the thyrotoxic phase of PPT

POSTPARTUM THYROIDITIS

treatment

Thyrotoxic phase:

symptomatic women may be treated with β-blockers

ATDs are not recommended

Following the resolution of the thyrotoxic phase, serum TSH should be measured in approximately 4–8 weeks (or if new symptoms develop) to screen for the hypothyroid phase.

Hypothyroid phase:

LT4 should be considered for women with **symptomatic** hypothyroidism due to PPT.

If treatment is not initiated, their TSH level should be checked every 4–8 weeks until thyroid function normalizes.

If **LT4** is initiated for PPT, **discontinuation of therapy** should be attempted after 12 months.

Thank you

for your attention