Indian Fertility Society

Synapse

3rd Edition

Hypothyroidism & Pregnancy

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The thyroid gland controls rate of metabolic processes throughout the body via the production of two hormones triiodothyronine (T3) and thyroxine (T4). As the function of the thyroid gland is under the control of the hypothalamo-pituitary axis, changes in thyroid function can impact greatly on reproductive function before, during and after conception. Thyroid disease is classically divided into hyperthyroidism and hypothyroidism, and the causes of thyroid disease are numerous\ **(Table 1).**[1]

Primary Hypothyroidism	Secondary Hypothyroidism	Tertiary Hypothyroidism
Autoimmune Diseases: Atrophic Thyroiditis Hashimotos Thyroiditis	Pituitary Failure Pituitary Tumor	Hypothalamic Failure
Iatrogenic: Radioiodine therapy Thyroidectomy Antithyroid drugs		
Transient: Subacute Thyroiditis Postpartum Thyroiditis		
Iodine Deficiency		

Normal pregnancy is associated with an increase in renal iodine excretion, an increase in thyroxine binding proteins, an increase in thyroid hormone production and thyroid stimulatory effects of hCG, human Chorionic Gonadotropin (reduction in serum TSH,Thyroid Stimulating Hormone).Following conception, circulating thyroxine binding globulin (TBG) and total T4 concentrations increase by 7 week of gestation and reach a peak by 16 week of gestation and remain high until delivery.

Hypothyroidism in pregnancy is a common condition with overt disease affecting approximately 0.5% of women, and subclinical disease approximately 2.5%.When iodine nutrition is adequate, **the most frequent cause of hypothyroidism is autoimmune thyroid disease (Hashimoto's thyroiditis).** The thyroid autoantibodies can be detected in approximately 30%–60% of pregnant women with an elevated TSH concentration.[2]
Both overt and subclinical hypothyroidism are associated with an increased risk of adverse obstetric and neonatal outcomes **(Table 2).**[1]

Table 2: Complications of Hypothyroidism in Pregnancy[1]

Maternal	Neonatal
Anemia	Fetal Distress in labor
Post Partum Haemorrhage	Prematurity/Low birth weight
Cardiac Dysfunction	Congenital Malformations
Preeclampsia	Perinatal Death
Placental abruption	Still Birth/Neurodevelopmental delay

Screening
The universal screening for abnormal TSH concentrations in early pregnancy is not recommended. At present a high-risk screening approach is currently adopted, therefore women at high risk **(Table 3)** should be screened.[2]

Table 3: Risk Factors for Thyroid Dysfunction[2]

Family/ Personal history of thyroid dysfunction/thyroid surgery
Goitre
Positive thyroid auto antibodies (anti TPO)
Diabetes type 1/Other autoimmune diseases
Clinical signs and symptoms of hypothyroidism

History of miscarriage/Preterm delivery
History of subfertility
History of therapeutic head and neck irradiation
Age ≥ 30years/Morbid obesity (BMI ≥40Kg/m^2)
Previous treatment with Amiodarone/Lithium
Recent exposure to iodinated radiological contrast agent
Residing in an area of known moderate or severe iodine insufficiency

Anti TPO: Thyroid Peroxidase antibodies

Diagnosis

The hypothyroidism during pregnancy is diagnosed by measuring serum TSH and serum T4.

Primary overt maternal hypothyroidism is defined as the presence of an elevated serum TSH and a decreased serum FT4 (Free Thyroxine) concentration during gestation, with both concentrations outside the (trimester-specific) reference ranges **(Table 4)**[2]
Subclinical hypothyroidism is defined as presence of an elevated serum TSH and normal serum FT4 concentration during gestation.

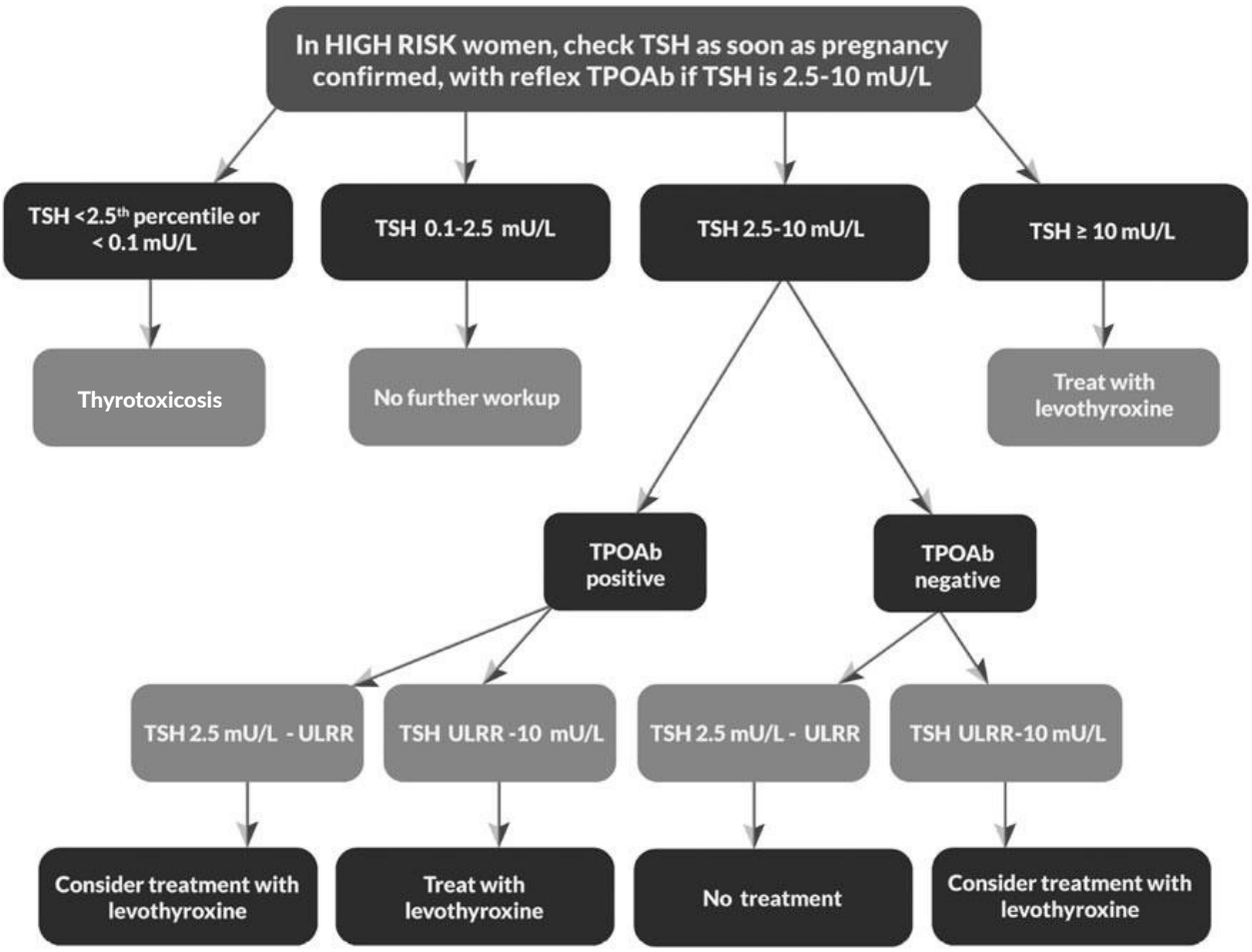
Table 4: Trimester Specific TSH Reference Ranges[2]

Trimester	TSH reference range
First (7-12 weeks)	The lower reference range of TSH can be reduced by approximately 0.4 mU/L, while the upper reference range is reduced by approximately 0.5mU/L (corresponds to 4mU/L).
Second and Third Trimesters	Nonpregnant Range (0.5mU/L to 4.5-5mU/L)

Treatment (Figure 1)[2]

The oral Levothyroxine (LT4) is drug of choice for treatment of hypothyroidism in pregnancy.
The dose of LT4 is increased by 20%-30% in hypothyroid patients receiving LT4 treatment with a suspected or confirmed pregnancy (e.g., positive home pregnancy test).[2]

Figure 1: Testing and Treatment of Hypothyroidism in Pregnancy, ULRR (Upper Limit of the Reference Range)[2]



To summarize, If TPOAb positive consider treatment if serum TSH is more than 2.5mU/L and if TPOAb negative consider treatment if TSH is more than ULRR.

Monitoring During Pregnancy:

Women with overt and subclinical hypothyroidism (treated or untreated) or those at risk for hypothyroidism {e.g. patients who are euthyroid but TPOAb (Thyroid Peroxidase antibody or TgAb Thyroglobulin antibodies) positive} should be monitored with a serum TSH measurement **approximately every 4 weeks until midgestation and at least once near 30 weeks gestation.[2]**

Postpartum:

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.[2]

Hypothyroidism and Infertility

Hypothyroidism affects the pulsatile release of gonadotrophin-releasing hormone, which is required for cyclical release of follicle-stimulating hormone and luteinising hormone and subsequent ovulation. Hypothyroidism in childhood and adolescence is associated with a delay in reaching sexual maturity and in adulthood is associated with menstrual disturbances (like oligomenorrhoea, menorrhagia and amenorrhoea). Hypothyroidism also alter the feedback to the pituitary by changing estrogen metabolism and circulating levels of sex hormone-binding globulin.[1]

Evaluation of serum TSH concentration is recommended for all women seeking care for infertility. LT4 treatment is recommended for infertile women with overt hypothyroidism who desire pregnancy.[2]

The prevalence of thyroid autoimmunity is higher among infertile patients, especially when infertility is caused by endometriosis or ovulatory dysfunction. There is fair evidence that thyroid autoimmunity is associated with infertility. LT4 may improve pregnancy outcomes in female with positive thyroid antibodies especially if serum TSH is > 2.5 mIU/L.[3]

The overt hypothyroidism affects the semen parameters as well as sexual behavior.The treatment with LT4 has significant improvement in semen parameters and sexual behavior. The subclinical hypothyroidism does not affect the semen parameters.[4]

Hypothyroidism and Recurrent Miscarriage[5]

Women with recurrent miscarriage should be offered thyroid function tests and assessment for thyroid peroxidase (TPO) antibodies.
Thyroxine supplementation is not routinely recommended for euthyroid women with TPO who have a history of miscarriage.

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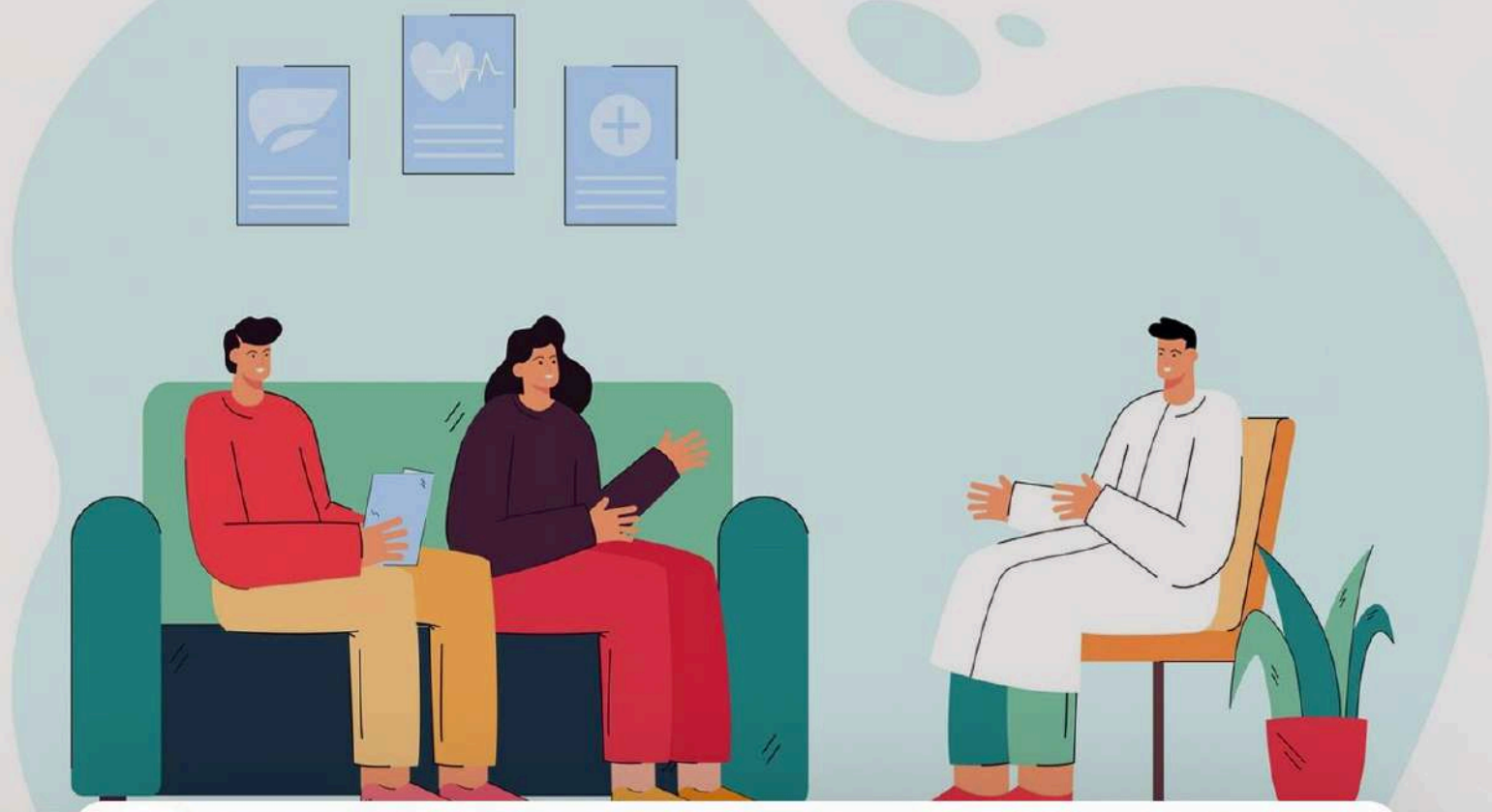

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