Diagnosis and Management of Thyroid Dysfunction in Pregnant Women: A Clinical Review

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***Abstract*—Background: Thyroid dysfunction is a common endocrine disorder during pregnancy and is associated with significant maternal and fetal complications if not appropriately managed. Physiological changes, including increased thyroxine-binding globulin and human chorionic gonadotropin-mediated suppression of thyroid-stimulating hormone, alter thyroid function tests and complicate diagnosis.**
Objective: This review aims to provide a comprehensive overview of the diagnosis and management of thyroid dysfunction in pregnant women, highlighting current clinical guidelines and recent advances.
Methods: A narrative review of published literature was conducted using peer-reviewed articles, clinical guidelines, and review papers focusing on thyroid disorders in pregnancy. Relevant data on epidemiology, physiological changes, diagnostic criteria, and management strategies were analyzed and synthesized.
Conclusion: Early diagnosis using trimester-specific reference ranges and appropriate therapeutic interventions are essential to maintain maternal euthyroidism and optimize fetal outcomes.

***Index Terms*—Thyroid dysfunction, Pregnancy, Hypothyroidism, Hyperthyroidism, Levothyroxine, Graves' disease, TSH**

I. INTRODUCTION

The thyroid gland is a highly vascularized endocrine organ located in the anterior region of the neck, extending from the fifth cervical (C5) to the first thoracic (T1) vertebrae. It lies beneath the platysma, sternohyoid, and sternothyroid muscles and consists of two lateral lobes connected by an isthmus. The gland typically weighs 15–20 g in adults and has a soft, reddish-brown appearance. Each lobe measures approximately 4 cm in length, 2 cm in width, and 2–3 cm in thickness, while the isthmus measures about 2 cm in breadth and 2–6 mm in thickness [1,2].

The thyroid gland is supplied by the superior and inferior thyroid arteries, and occasionally by an additional vessel known as the thyroidea ima artery [1]. It plays a vital role in regulating metabolism, growth, and development through the secretion of thyroid hormones, primarily thyroxine (T4) and triiodothyronine (T3).

Pregnancy induces significant physiological changes in thyroid function. Increased estrogen levels lead to a rise in thyroxine-binding globulin (TBG), resulting in approximately a 50% increase in total T3 and T4 concentrations [3,7,8]. Additionally, human chorionic gonadotropin (hCG) stimulates the thyroid gland, leading to transient suppression of thyroid-stimulating hormone (TSH), particularly during the first trimester [10,32]. These physiological alterations necessitate the use of trimester-specific reference ranges for accurate interpretation of thyroid function tests during pregnancy [6,20].

Thyroid disorders are among the most common endocrine conditions affecting women of reproductive age. Autoimmune thyroid diseases, including Hashimoto's thyroiditis and Graves' disease, are significantly more prevalent in women, with a female-to-male ratio of approximately 8–10:1 [10,11]. The prevalence of hypothyroidism during pregnancy is estimated to be around 4% (0.5% overt and 3.5% subclinical), while hyperthyroidism affects approximately 2.4% of pregnancies [4,11].

If left undiagnosed or inadequately managed, thyroid dysfunction during pregnancy can lead to adverse maternal and fetal outcomes, including miscarriage, preterm birth, and impaired neurodevelopment [5,15]. Therefore, early detection, accurate diagnosis, and appropriate management of thyroid disorders during pregnancy are essential to ensure optimal health outcomes for both the mother and the fetus.

1.1 Physiological Changes of the Thyroid in Pregnancy

Pregnancy is associated with significant physiological alterations in thyroid function, primarily driven by hormonal and metabolic changes. These adaptations are essential to meet the increased metabolic demands of the mother and to ensure adequate thyroid hormone supply for fetal development [7,10].

One of the earliest changes during pregnancy is the rise in estrogen levels, which leads to an increase in thyroxine-binding globulin (TBG). This results in elevated total thyroxine (T4) and triiodothyronine (T3) concentrations, typically by approximately 30–50% above pre-pregnancy levels [3,8]. Despite this increase in total hormone levels, free hormone concentrations (FT4 and FT3) remain relatively stable due to physiological regulatory mechanisms [8,24].

Human chorionic gonadotropin (hCG), structurally similar to thyroid-stimulating hormone (TSH), exerts a stimulatory effect on the thyroid gland. This leads to a transient increase in free thyroxine (FT4) levels and a corresponding suppression of TSH, particularly during the first trimester [32]. As pregnancy progresses, hCG levels decline, and TSH levels gradually return toward normal ranges [10].

Pregnancy is also associated with increased iodine requirements due to enhanced renal clearance, increased maternal thyroid hormone production, and transfer of iodine to the fetus. Consequently, daily iodine requirements increase by approximately 50% during pregnancy [27,30]. In iodine-deficient regions, this may lead to thyroid enlargement (goiter), with an increase in thyroid gland size of up to 20–40%, compared to approximately 10% in iodine-sufficient areas [7,27].

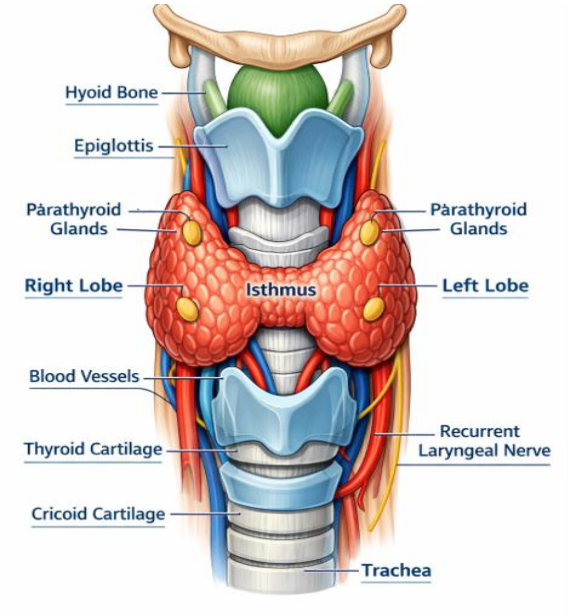

Fig. No. 1 Physiology of Thyroid Gland

Additionally, placental deiodinase enzymes, particularly type 3 deiodinase, play a critical role in regulating fetal exposure to thyroid hormones by converting T4 into inactive metabolites. This further contributes to increased maternal thyroid hormone production during pregnancy [10].

Due to these physiological changes, the normal reference range for TSH is lower during pregnancy compared to non-pregnant individuals. Trimester-specific reference ranges are therefore essential for accurate diagnosis, with an upper limit of approximately 2.5 mIU/L in the first trimester and 3.0 mIU/L in the second and third trimesters [20,23].

Overall, these complex physiological adaptations ensure adequate availability of thyroid hormones for both maternal metabolic needs and optimal fetal growth and neurodevelopment.

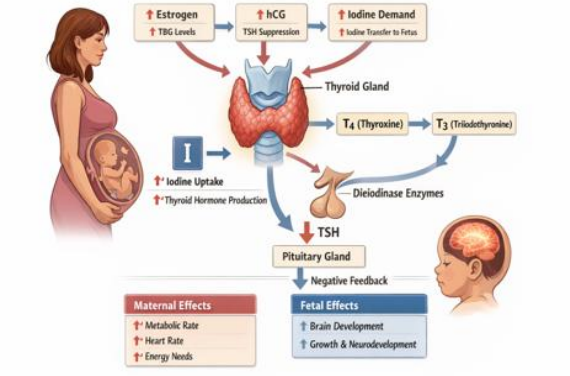

Fig No. 2 Thyroid Physiology in Pregnancy

II. HYPOTHYROIDISM

Hypothyroidism is one of the most common thyroid disorders encountered during pregnancy. Population studies indicate that approximately 2–3% of pregnant women have undiagnosed hypothyroidism, with the majority (≈2/3) presenting as subclinical hypothyroidism [16,18]. Subclinical hypothyroidism is defined biochemically as an elevated serum thyroid-stimulating hormone (TSH) with normal free thyroxine (FT4) levels, whereas overt hypothyroidism presents with elevated TSH accompanied by reduced FT4 [16,18].

2.1 Etiology:

The predominant cause of hypothyroidism during pregnancy is autoimmune thyroiditis (Hashimoto's thyroiditis), characterized by progressive destruction of thyroid tissue mediated by autoantibodies against thyroid peroxidase (TPO) and thyroglobulin (TG) [13,14]. Other less common causes include iodine deficiency, previous thyroid surgery, or radioactive iodine therapy prior to conception [7,10].

2.2 Clinical Presentation:

Hypothyroidism in pregnancy often has nonspecific or subtle symptoms that overlap with normal pregnancy changes, such as fatigue, weight gain, constipation, and cold intolerance. Consequently, biochemical screening is crucial, as only 20–30% of women with overt hypothyroidism present with classical symptoms [16]. Subclinical hypothyroidism is typically asymptomatic and usually detected through targeted or universal screening protocols [19,20].

III. HYPERTHYROIDISM

Hyperthyroidism affects approximately 0.2–0.7% of pregnancies, with Graves' disease (GD) being the most frequent etiology [23,25]. Hyperthyroidism can be overt or subclinical.

3.1 Clinical Features

Overt hyperthyroidism presents with palpitations, heat intolerance, weight loss despite increased appetite, tremors, and anxiety. Subclinical hyperthyroidism is typically asymptomatic and characterized by suppressed TSH with normal FT4 and FT3 levels [23,31].

3.2 Etiology

1. Graves' Disease (GD): Autoimmune stimulation of the thyroid by TSH receptor antibodies (TRAb) [24].
2. Toxic multinodular goiter and toxic adenoma: Rare but may cause overt hyperthyroidism [23].
3. Transient forms: Thyroiditis, including postpartum thyroiditis [39].
4. Other causes: Molar pregnancy, exogenous thyroid hormone ingestion, iodine-induced hyperthyroidism [23,25].

IV. DIAGNOSIS

4.1 Hypothyroidism

Accurate diagnosis relies on trimester-specific reference ranges for thyroid function tests (TFTs) [20,23].

- Primary screening: Serum TSH measurement.
- Further evaluation: If TSH is above the trimester-specific upper limit (or >4 mIU/L if reference ranges are unavailable), serum FT4 should be measured to differentiate between subclinical and overt hypothyroidism [16,18,20].
- Autoimmune confirmation: Detection of anti-TPO and anti-TG antibodies confirms autoimmune etiology [13,14].

4.2 Hyperthyroidism

- Serum TSH: Low TSH suggests hyperthyroidism; FT4 and FT3 measured accordingly [22,23].
- TRAb Levels: Confirm Graves' disease and assess fetal risk [24,26].
- Imaging: Ultrasound is safe; radionuclide studies are contraindicated [28,29].
- Iodine Uptake Studies: Not performed during pregnancy [23,27].

4.3 Maternal and Fetal Risks:

- Untreated hypothyroidism in pregnancy is associated with adverse outcomes including miscarriage, preeclampsia, preterm birth, low birth weight, and impaired fetal neurodevelopment [5,18,34]. Early identification and treatment are essential to prevent these complications.

4.4 Maternal and Fetal Risks

- Untreated hyperthyroidism may cause preeclampsia, heart failure, thyroid storm, miscarriage [25,39]. Fetal risks include intrauterine growth restriction, preterm birth, low birth weight, and fetal/neonatal thyrotoxicosis [24,26].

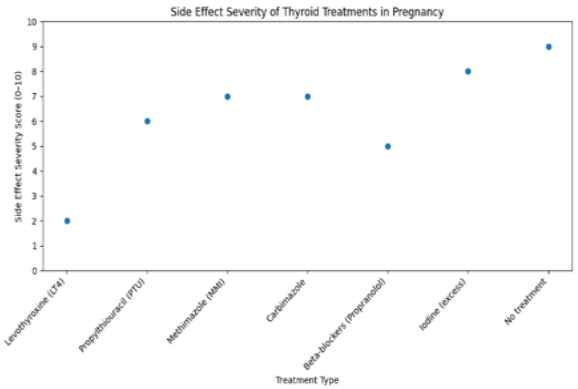

Fig No. Side Effect Severity Profile of Thyroid Treatments in Pregnancy

V. MANAGEMENT OF HYPOTHYROIDISM:

The management of hypothyroidism during pregnancy primarily involves levothyroxine (LT4) replacement therapy, which is considered the standard and most effective treatment for overt hypothyroidism. In women already receiving LT4 prior to conception, an early pregnancy dose adjustment is often necessary, with an increase of approximately 30–50% to meet the heightened physiological demand for thyroid hormones and to maintain euthyroid status throughout gestation [35]. In cases of subclinical hypothyroidism, treatment decisions are more individualized and depend on both biochemical values and immunological status. LT4 therapy is generally recommended when serum TSH levels are equal to or exceed 4 mIU/L, or when anti-thyroid peroxidase (anti-TPO) antibodies are positive, as these conditions are associated with increased risks of miscarriage, adverse pregnancy outcomes, and impaired fetal neurodevelopment [36,37]. Alongside pharmacological therapy, adequate iodine intake plays a crucial preventive role in maternal and fetal thyroid health. A daily iodine supplementation of approximately 150 µg is recommended, especially in iodine-deficient regions, to support normal thyroid hormone synthesis; however, excessive iodine intake should be strictly avoided as it may lead to thyroid dysfunction in both mother and fetus [27,30].

VI. MANAGEMENT OF HYPERTHYROIDISM:

Management of hyperthyroidism in pregnancy, particularly Graves' disease, requires trimester-specific and carefully balanced pharmacological therapy to ensure maternal control while minimizing fetal risk. In the first trimester, propylthiouracil (PTU) is preferred due to its comparatively safer fetal profile, whereas methimazole (MMI) or carbimazole is recommended during the second and third trimesters to reduce the risk of hepatotoxicity associated with prolonged PTU use [39,40]. Across all stages of pregnancy, the treatment strategy emphasizes administering the lowest effective dose of antithyroid drugs to maintain maternal free thyroxine (FT4) levels in the upper-normal physiological range, thereby preventing both maternal thyrotoxicosis and fetal hypothyroidism [40]. For symptomatic management, short-term use of beta-adrenergic blockers such as propranolol may be employed to control manifestations like tachycardia, palpitations, and tremors, although their use is generally limited due to potential fetal effects with prolonged therapy [41]. In severe cases such as thyroid storm, an emergency condition requiring immediate intervention, hospitalization is essential, and management typically involves a combination of antithyroid medications, iodine administration, beta-blockers, corticosteroids, and intensive supportive care to stabilize the patient [39,41]. Postpartum thyroiditis is usually a transient condition that may present with a hyperthyroid phase followed by hypothyroidism; in such cases, beta-blockers are used for symptomatic relief during hyperthyroidism, while levothyroxine (LT4) therapy is initiated if hypothyroid symptoms persist or become clinically significant [40,41].

Table No.1 Trimester-wise Thyroid Reference Values (43)

Parameter	1st Trimester	2nd Trimester	3rd Trimester
TSH (mIU/L)	0.1 – 2.5	0.2 – 3.0	0.3 – 3.0
Free T4	Slight ↑	Normal	Slight ↓
Total T4	↑ (30–50%)	↑	↑
TBG	↑↑	↑↑	↑↑

Table No.2 Clinical Management of Hypothyroidism and Hyperthyroidism. (42)

Thyroid Disorder	First-Line Treatment	Notes
Overt Hypothyroidism	Levothyroxine (T4)	Normalize TSH; adjust dose every 6–8 weeks
Subclinical Hypothyroidism	Consider Levothyroxine if TSH >10 mIU/L or symptomatic	Monitor TSH and T4 regularly
Hyperthyroidism (Graves' disease)	Antithyroid drugs (Methimazole preferred), Radioactive iodine (RAI), Surgery	Choice depends on age, pregnancy, comorbidities
Symptomatic Control in Hyperthyroidism	Beta-blockers (Propranolol)	Controls adrenergic symptoms
Thyroid Storm	High-dose antithyroid drugs + supportive care	Life-threatening; requires ICU management
Post-Ablative Hypothyroidism	Lifelong Levothyroxine	Required after surgery or RAI

VII. MONITORING

- Regular biochemical monitoring ensures safety for mother and fetus [35,36].
- TRAb testing for women with Graves' disease [24,26].
- Postpartum dose adjustment of antithyroid drugs and LT4 as needed [39,41].

Key Principle: Maintain maternal euthyroidism while minimizing adverse fetal outcomes [34–41].

VIII. FUTURE DIRECTIONS

Recent research highlights several important gaps and future directions in the management of thyroid disorders in pregnancy. Population-specific reference ranges for thyroid-stimulating hormone (TSH) and free thyroxine (FT4) are essential, as physiological variations across different populations can significantly affect diagnostic accuracy and clinical decision-making [23,36]. In addition, the long-term effects of subclinical hypothyroidism on offspring remain insufficiently understood and require further longitudinal studies to clarify developmental and metabolic outcomes [37,40]. Emerging biomarkers such as serum thyroglobulin, deiodinase enzyme activity, and circulating microRNAs show potential for improving diagnostic precision; however, these novel indicators still require extensive validation before routine clinical application [31]. Advanced analytical techniques like liquid chromatography–tandem mass spectrometry (LC–MS/MS) have demonstrated improved sensitivity and accuracy in hormone measurement, offering advantages over conventional immunoassays [33]. Furthermore, the integration of digital health technologies and artificial intelligence may enhance risk stratification, early detection, and continuous monitoring of thyroid dysfunction in pregnancy [35]. Current evidence also indicates the need for robust clinical trials to compare universal versus targeted screening strategies for better maternal–fetal outcomes [21]. Finally, there is a clear requirement for standardized treatment protocols, particularly for subclinical thyroid disorders, to ensure consistency in clinical practice and improve patient outcomes [34,36].

IX. CONCLUSION

Thyroid dysfunction in pregnancy is common and clinically significant [6,10,11]. Physiological changes such as increased TBG and hCG-mediated TSH suppression necessitate trimester-specific reference ranges [7,23,24]. Early detection and targeted therapy with LT4 for hypothyroidism and antithyroid drugs for hyperthyroidism maintain maternal euthyroidism and optimize fetal outcomes [34, 42]. Regular biochemical monitoring is crucial [41]. Future research will enhance diagnosis, management, and prognosis [36,41]. Evidence-based strategies are essential to improve maternal and fetal health.

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