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Management of Hyperthyroidism in Pregnancy: Implications for Maternal and Fetal Outcomes

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Abstract

Background: Hyperthyroidism in pregnancy, while uncommon, poses significant risks to both maternal and fetal health. The most prevalent cause is Graves' disease, an autoimmune disorder driven by thyroid-stimulating antibodies (TRAbs) that can cross the placenta. Physiological changes of pregnancy often mask or mimic symptoms of thyrotoxicosis, complicating diagnosis and potentially delaying treatment.

Aim: This review aims to synthesize the etiology, pathophysiology, and evidence-based management of hyperthyroidism in pregnancy. It emphasizes optimizing maternal and fetal outcomes through timely diagnosis, appropriate treatment, and vigilant monitoring.

Methods: A comprehensive review of the clinical approach is presented, covering the initial evaluation using trimester-specific thyroid function tests, the role of TRAb measurement for diagnosis and fetal risk stratification, and the management principles using antithyroid drugs (ATDs). The importance of fetal surveillance through ultrasound and heart rate monitoring is also detailed.

Results: Proper management, primarily with antithyroid drugs, significantly improves outcomes. A treatment strategy of Propylthiouracil (PTU) in the first trimester, transitioning to Methimazole (MMI) thereafter, balances the risks of teratogenicity and hepatotoxicity. Uncontrolled disease is linked to miscarriage, preeclampsia, and fetal thyrotoxicosis, while overtreatment can cause fetal hypothyroidism. Fetal surveillance is critical when maternal TRAbs are elevated.

Conclusion: Successful management of hyperthyroidism in pregnancy requires a multidisciplinary approach to maintain maternal euthyroidism with the lowest effective ATD dose, while conducting ongoing fetal assessment to mitigate complications.

Keywords: Hyperthyroidism, Pregnancy, Graves' Disease, Antithyroid Drugs, Propylthiouracil, Methimazole, Fetal Surveillance, Thyrotropin Receptor Antibodies (TRAbs).

Introduction

Hyperthyroidism in pregnancy is a relatively uncommon endocrine disorder, yet it carries significant clinical implications for both mother and fetus.[1] It is defined biochemically by increased circulating concentrations of thyroxine (T4) and triiodothyronine (T3) with a suppressed serum thyroid-stimulating hormone (TSH), reflecting excessive thyroid hormone production and negative feedback on the hypothalamic–pituitary axis.[1] The most frequent cause in women of childbearing age is Graves' disease, although other etiologies such as toxic multinodular goiter and transient gestational thyrotoxicosis may also be encountered.[2] Because the physiological changes of pregnancy can mask or mimic symptoms of thyrotoxicosis, such as palpitations, heat intolerance, and fatigue, the diagnosis may be challenging and thus delayed.[2] Despite its low prevalence compared with other obstetric conditions, timely recognition and management of overt hyperthyroidism are crucial to reducing the risk of serious complications. Uncontrolled maternal hyperthyroidism has been associated with miscarriage, preeclampsia, heart failure, preterm birth, fetal growth restriction, and fetal or neonatal thyrotoxicosis.[2] From a public health perspective, the fact that a substantial proportion of pregnancies are unplanned underscores the importance of preconception counseling and routine screening in high-risk women to detect thyroid dysfunction before or early in gestation.[3] Achieving and maintaining a euthyroid state prior to conception is ideal; however, in real-world practice many women first present after conception, necessitating careful assessment and rapid therapeutic decision-making.[3] This review focuses on the etiology, epidemiology, and pathophysiological mechanisms underlying hyperthyroidism during pregnancy, emphasizing the complex interplay between pregnancy-induced immunologic and hormonal changes and preexisting thyroid disease.[1] It also outlines an evidence-based approach to the initial clinical and laboratory

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evaluation, including the interpretation of trimester-specific reference ranges for TSH and free thyroid hormones.[2] Subsequent sections will discuss available treatment modalities, such as antithyroid drugs and adjunctive therapies, as well as nursing roles in monitoring, education, and multidisciplinary coordination of care to optimize maternal and fetal outcomes.[3]

Etiology:

Thyroid disorders are the second most prevalent endocrine conditions observed during pregnancy, reflecting the substantial physiological impact of gestation on thyroid function and immune regulation.[4] Among these disorders, hyperthyroidism requiring active medical management is most frequently attributable to Graves' disease, which is estimated to account for approximately 85% to 95% of clinically significant cases of hyperthyroidism in pregnancy.[2][3][5][6] This predominance is explained by the fact that Graves' disease typically affects women of reproductive age and may either first present, worsen, or relapse during pregnancy due to shifts in immune tolerance and hormonal milieu.[2][3] Graves' disease is an autoimmune condition in which loss of immune tolerance leads to the production of thyrotropin-receptor antibodies (TRAb) directed against the TSH receptor on thyroid follicular cells.[6] These antibodies mimic the action of TSH by binding to and persistently activating the receptor, thereby stimulating unregulated synthesis and secretion of thyroxine (T4) and triiodothyronine (T3).[6] The continuous receptor activation drives diffuse thyroid hyperplasia and goiter formation, resulting in the clinical manifestations of thyrotoxicosis such as weight loss, palpitations, heat intolerance, and tremor, which may overlap with normal pregnancy symptoms and complicate diagnosis.[2][5][6] Importantly, TRAb are IgG antibodies capable of crossing the placenta, so maternal autoimmunity can also affect the fetal and neonatal thyroid gland, predisposing to fetal or neonatal hyperthyroidism even when the mother has been treated or appears clinically euthyroid.[6] Although other causes of hyperthyroidism, such as toxic multinodular goiter or transient gestational thyrotoxicosis, may occur, they represent a much smaller proportion of cases compared with Graves' disease in the pregnant population.[2][3][5] Consequently, understanding the autoimmune etiology and antibody-mediated mechanisms underlying Graves' disease is central to the evaluation, risk stratification, and multidisciplinary management of hyperthyroidism during pregnancy, with implications not only for maternal health but also for fetal surveillance and neonatal outcomes.[4][6]

Epidemiology

The epidemiology of hyperthyroidism in pregnancy reflects both the natural age distribution of thyroid disease and the physiological changes associated with gestation. Graves' disease, the leading cause of hyperthyroidism in women of reproductive age, has an overall prevalence of approximately 0.5% in the general population, underscoring its relative rarity but clinical relevance.[7] During pregnancy, the incidence of hyperthyroidism is estimated to be between 0.1% and 0.2%, making it an uncommon but important condition requiring careful monitoring due to its potential maternal and fetal consequences.[8] The disorder most frequently affects women between 20 and 40 years of age, a demographic that overlaps significantly with peak reproductive years, and evidence suggests that the incidence steadily increases with advancing maternal age within this range.[1] In contrast to Graves' disease, clinically significant hyperthyroidism resulting from non-autoimmune causes is far less common in pregnancy. For instance, hyperthyroidism secondary to autonomously functioning thyroid nodules—whether single toxic adenomas or multinodular goiters—occurs very infrequently in individuals under 40 years old, with estimated incidence rates of less than 0.001% to 0.002% in this age group.[9] This disparity emphasizes the dominant role of autoimmune mechanisms in pregnant populations and highlights the importance of distinguishing Graves' disease from other etiologies through careful clinical assessment and laboratory evaluation.[7][9] Geographic and nutritional factors also influence prevalence patterns. In regions with endemic iodine deficiency, the prevalence of hyperthyroidism tends to be higher due to the compensatory development of functional thyroid nodules capable of producing excess thyroid hormone.[5] These nodules may become hyperactive under the stimulatory influence of pregnancy-related hormonal changes, thereby increasing the likelihood of thyrotoxicosis in affected areas.[5] Overall, understanding the epidemiological distribution of hyperthyroidism in pregnancy is essential for targeted screening, early recognition, and the development of context-specific public health strategies to reduce maternal and neonatal complications.

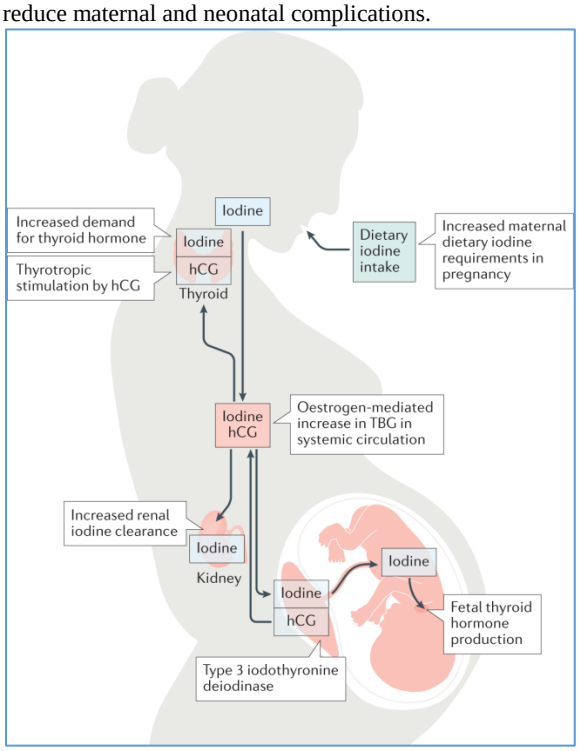

Figure-1: Thyroid Disorders in Pregnancy.

Pathophysiology

The pathophysiology of hyperthyroidism in pregnancy is shaped by the complex interplay between normal gestational physiology and underlying thyroid disease. Pregnancy induces substantial hormonal, metabolic, and immunologic shifts that influence thyroid function and can either mask, mimic, or exacerbate preexisting hyperthyroidism. One of the earliest and most significant changes is the estrogen-driven rise in thyroxine-binding globulin (TBG). Elevated estrogen levels increase hepatic synthesis of TBG by approximately 50%, leading to

greater binding of circulating thyroxine (T4) and a transient reduction in free T4 concentrations.[2][8][9][10] To maintain euthyroidism, the maternal thyroid gland undergoes adaptive hypertrophy and upregulates production of both T4 and triiodothyronine (T3), effectively doubling hormone output compared to the non-pregnant state. This physiological adjustment explains why women with limited thyroidal reserve, untreated disease, or iodine deficiency may become symptomatic during pregnancy.[2][9] Another key mechanism involves human chorionic gonadotropin (hCG), which peaks in the first trimester. Because hCG shares structural homology with thyroid-stimulating hormone (TSH), particularly in its alpha subunit, it can bind the TSH receptor and stimulate the thyroid gland. This receptor cross-reactivity results in increased free T4 levels and contributes to a physiologic suppression of TSH during early gestation.[5][7][9][11] In some women, especially those with heightened sensitivity to hCG or very high hCG levels—as seen in multiple gestations or hyperemesis gravidarum—this effect can lead to transient gestational thyrotoxicosis. While typically self-limited, this condition must be distinguished from pathological causes of hyperthyroidism, particularly Graves' disease.[9][11]

The pathophysiology of Graves' disease during pregnancy is fundamentally autoimmune. Thyrotropin receptor antibodies (TRAbs) interact with the TSH receptor on thyroid follicular cells and may exert either stimulating or blocking effects. In Graves' disease, the predominant stimulatory action of TRAbs results in excessive production of free T4 and T3, often requiring pharmacologic control.[2][3][5][9] Pregnancy itself induces a relative immune suppression to prevent fetal rejection, and this immunologic shift contributes to decreasing TRAb titers as pregnancy progresses, particularly in the second and third trimesters.[2] However, after childbirth the immune system rebounds toward a heightened inflammatory state, leading to increased TRAb concentrations and consequently raising the risk of postpartum relapse of Graves' hyperthyroidism or the development of postpartum thyroiditis.[2][10] The placenta further modifies maternal thyroid physiology through expression of deiodinase type 3 (D3), an enzyme responsible for inactivating T4 and T3 by converting them into inactive metabolites. Overactivity of D3 can theoretically induce maternal hypothyroidism, although in most pregnancies this effect is offset by the strong thyrotropic action of hCG in early gestation.[9][12] As hCG levels peak and subsequently decline by midpregnancy, free T4 levels gradually normalize and TSH stabilizes within gestation-specific ranges. These dynamic physiologic changes create a fluctuating endocrine environment that can significantly influence the presentation, severity, and management of hyperthyroidism in pregnancy, underscoring the importance of trimester-specific interpretation of thyroid function tests and individualized clinical care.[8][9][12]

History and Physical

The clinical assessment of hyperthyroidism during pregnancy requires careful differentiation between normal gestational changes and true pathological findings, as many symptoms overlap significantly. Pregnancy itself induces physiologic alterations such as increased heart rate, mild dyspnea, heat intolerance, and heightened metabolic demand, all of which may resemble manifestations of thyrotoxicosis.[5][9] This overlap often complicates early recognition and may delay diagnosis, making a thorough history and targeted physical examination essential. Beyond these shared features, hyperthyroidism typically presents with additional systemic symptoms, including diaphoresis, persistent heat intolerance, palpitations, insomnia, heightened nervousness, tremors, anxiety, pruritus, and increased appetite accompanied by paradoxical weight loss. Gastrointestinal hypermotility may result in frequent bowel movements, providing another distinguishing clue when present in excess of normal pregnancy-related changes.[5][9] Physical examination can further support diagnostic suspicion. A diffusely enlarged, non-nodular goiter is common in hyperthyroid states and particularly associated with Graves' disease, the predominant cause of hyperthyroidism in pregnancy. Persistent tachycardia widened pulse pressure, and sometimes hypertension may also be noted upon evaluation.[1][3] The presence of extrathyroidal manifestations strongly suggests an autoimmune etiology. Ophthalmopathy—manifesting as exophthalmos or proptosis—occurs in roughly 50% of individuals with Graves' disease, although its severity does not always correlate with biochemical thyroid status.[1][3][9] Dermatologic findings such as pretibial myxedema, although characteristic, are far less common, appearing in fewer than 10% of cases.[3][9] A detailed medical history is particularly important for pregnant individuals with a known or suspected thyroid disorder. Prior diagnosis of Graves' disease warrants close attention, even in those who have undergone definitive treatments such as thyroidectomy or radioiodine ablation. Thyrotropin receptor antibodies (TRAbs) may persist for years after such interventions, posing a continued risk of fetal or neonatal hyperthyroidism due to transplacental transfer of maternal IgG antibodies.[5][11] Because fetal thyroid dysfunction can occur even when the mother is euthyroid, documenting previous disease activity, treatment modalities, and antibody status is critical for planning fetal surveillance and maternal management. Thus, an integrative approach to history and physical examination plays a central role in the early detection, risk assessment, and multidisciplinary care of hyperthyroidism in pregnancy.

Evaluation

The evaluation of suspected new-onset hyperthyroidism in pregnancy follows similar principles to that of the nongravid patient but requires careful adaptation to the unique physiologic changes of gestation.[9] Initial assessment begins with measurement of serum thyroid-stimulating hormone (TSH), which serves as the most sensitive marker of thyroid dysfunction. However, interpretation during pregnancy is more challenging because TSH is often partially suppressed in early gestation due to human chorionic gonadotropin (hCG), which has thyrotropic activity and stimulates the maternal thyroid gland, leading to increased thyroid hormone production and subsequent negative feedback on TSH.[9][11] When a TSH value is found to be below the appropriate trimester-specific reference range, further testing of thyroid hormone levels is necessary to distinguish overt hyperthyroidism from normal pregnancy-related changes or subclinical disease. Free thyroxine (free T4) is most commonly evaluated in this context, although other parameters such as total T4, total T3, the free T4 index, and thyroxine-binding

globulin (TBG) concentrations can provide additional insight, especially when assay interferences or binding protein alterations are suspected.[5][11][12][13] A key element in the evaluation of thyroid function during pregnancy is the recognition that normal laboratory values differ from those of the nongravid state and vary across trimesters. Rising estrogen levels increase TBG concentrations, leading to higher total T4 and T3, necessitating pregnancy- and trimester-specific reference intervals.[9][13] Consequently, reliance on nonpregnant reference ranges can result in inappropriate labeling of euthyroid pregnant patients as hyperthyroid or hypothyroid.[7] Evidence-based guidelines recommend trimester-specific TSH reference ranges of approximately 0.1 to 2.5 mIU/L in the first trimester, 0.2 to 3.0 mIU/L in the second trimester, and 0.3 to 3.5 mIU/L in the third trimester.[7] Because free T4 assay performance is variable, individual laboratories are urged to establish their own pregnancy-adjusted reference ranges, ideally derived from healthy pregnant populations.[13]

Despite careful use of appropriate ranges, establishing a definitive diagnosis of hyperthyroidism may remain difficult due to the dynamic and fluctuating nature of thyroid physiology in pregnancy. In cases where biochemical results and clinical findings are borderline or discordant, it is reasonable to adopt a conservative approach and repeat thyroid function tests over time to observe trends, rather than initiating antithyroid drug therapy immediately.[12] This is particularly important given that subclinical hyperthyroidism, defined by suppressed TSH with normal free T4 and T3 levels, has not been clearly associated with adverse maternal or fetal outcomes, and therefore does not routinely warrant treatment.[7][8][10] Serial monitoring allows the clinician to differentiate transient, physiological TSH suppression from evolving overt hyperthyroidism that may necessitate pharmacologic intervention.[9][12] Immunologic testing is also central to the evaluation, particularly in differentiating Graves' disease from gestational transient thyrotoxicosis. Thyrotropin receptor antibodies (TRAbs) are usually detectable in Graves' disease and can serve as a diagnostic marker when the clinical picture is ambiguous.[2][5][11][13] The presence of TRAbs supports an autoimmune etiology, whereas their absence in the context of mild, self-limited biochemical hyperthyroidism early in pregnancy may suggest hCG-mediated gestational thyrotoxicosis.[5][11] However, most commonly used TRAb assays measure total binding antibodies and do not distinguish between stimulatory and inhibitory subtypes.[9] In highly complex or inconclusive cases, more specialized bioassays capable of identifying specifically stimulatory TRAbs may be employed to refine the diagnosis.[9] Beyond initial diagnosis, TRAb measurement has important implications for fetal risk stratification. The American Thyroid Association and the Endocrine Society recommend measuring TRAbs between 20 and 24 weeks of gestation in women with current or past Graves' disease, a history of positive TRAbs, previous neonates affected by Graves' disease, or recent radioiodine ablation or thyroidectomy.[2][3][5][13] Even in women who are clinically euthyroid or hypothyroid following definitive therapy, persistent maternal TRAbs can cross the placenta and stimulate the fetal thyroid, potentially leading to fetal or neonatal hyperthyroidism.[5][11] Therefore, appropriate immunologic evaluation not only informs maternal management but also guides the need for targeted fetal surveillance, multidisciplinary counseling, and neonatal planning.

Treatment / Management

The management of hyperthyroidism in pregnancy is centered on achieving and maintaining maternal euthyroidism while minimizing risks to the fetus. Pharmacologic therapy with antithyroid drugs (ATDs) remains the cornerstone of treatment, as these agents directly inhibit thyroid hormone synthesis and thereby mitigate the deleterious cardiovascular and metabolic consequences of thyrotoxicosis.[2][3][5][9] The thioamide drugs most widely used in clinical practice are propylthiouracil (PTU) and methimazole (MMI). Carbimazole, a prodrug converted to methimazole, is commonly prescribed outside North America and exhibits a similar spectrum of efficacy and adverse effects.[3][9][13] All ATDs cross the placenta and can influence fetal thyroid function, which necessitates careful dose titration and frequent biochemical monitoring throughout pregnancy.[2][5][6][8] Historically, PTU was preferentially used across all patient groups due to its additional inhibition of peripheral conversion of T4 to T3. However, accumulating evidence of severe hepatotoxicity, including fulminant hepatic failure requiring liver transplantation, has led to a shift in practice toward favoring methimazole for most nonpregnant and pregnant patients outside of early gestation.[2][5][11][15] The major exception is the first trimester, during which exposure to methimazole or carbimazole is associated with a rare but well-described embryopathy. This methimazole embryopathy encompasses a constellation of congenital anomalies such as aplasia cutis, abdominal wall defects, esophageal and choanal atresia, ocular abnormalities, urinary tract malformations, and various circulatory defects.[2][5][8][14] To reduce this teratogenic risk during the critical period of organogenesis, PTU is recommended as the first-line ATD in early pregnancy. Once organogenesis is largely complete—typically after the first trimester—patients are transitioned from PTU to methimazole to reduce cumulative PTU exposure and thereby decrease the likelihood of serious hepatotoxicity.[2][5][11][15] Although PTU is associated with fewer and generally milder congenital abnormalities than methimazole, these defects may be subtle and not recognized until later childhood. Examples reported at birth include unilateral renal dysgenesis or agenesis, situs inversus, and certain cardiac outflow tract anomalies, which tend to occur as isolated defects rather than the syndromic pattern observed with methimazole embryopathy.[7][11][12] In clinical practice, the risk–benefit balance favors short-term PTU use during early gestation followed by prompt transition to methimazole for ongoing control of maternal hyperthyroidism once the first trimester has concluded.[2][5][11][15]

Despite concerns over teratogenicity, treatment of overt hyperthyroidism during pregnancy is essential, as uncontrolled disease is associated with increased risks of miscarriage, preterm delivery, maternal heart failure, and fetal loss.[7][12] Importantly, untreated severe thyrotoxicosis itself has been linked to congenital anomalies, further underscoring that the risks of no therapy frequently exceed those of appropriately used ATDs.[15] When patients do not tolerate PTU, methimazole is generally preferred even in the first trimester rather than withholding therapy altogether, particularly in the setting of overt disease.[16] Because ATDs cross the placenta, they

can also treat fetal hyperthyroidism caused by maternal thyrotropin receptor antibodies (TRAbs); however, overtreatment may result in fetal hypothyroidism even if maternal thyroid function appears normal.[2][3][5][11] For this reason, the therapeutic goal is to administer the lowest effective ATD dose that maintains maternal free T4 at the upper limit of or slightly above the normal pregnancy-specific reference range, with TSH often remaining mildly suppressed.[2][3][5][11] A fully normalized or high-normal maternal TSH may indicate that the fetus is receiving excessive ATD exposure, prompting downward adjustment of the maternal dose.[9] Dosing strategies take into account the differing pharmacokinetics of PTU and methimazole. PTU has a shorter half-life and is typically administered in divided doses of 100 to 300 mg per day, usually split into three doses.[9] Methimazole, by contrast, has a longer duration of action and can be given once daily at doses ranging from 5 to 15 mg, depending on disease severity and biochemical response.[9] When transitioning from PTU to methimazole, a rough conversion ratio of 20:1 (PTU:mmimazole) is commonly used as a starting point, although subsequent titration must be guided by serial thyroid function testing.[5] Because of individual variability in drug metabolism and the evolving physiology of pregnancy, a temporary period of suboptimal control may occur during transitions, necessitating close follow-up and dose adjustments.[7]

Laboratory monitoring plays a central role in safe and effective management. After initiating, adjusting, or switching ATD therapy, thyroid function tests—typically TSH and free T4, with or without total T3—should be reassessed every 2 to 4 weeks until a stable euthyroid state is achieved.[3][11][13] Once control is established, the testing interval may be gradually extended, yet regular monitoring remains essential throughout pregnancy due to ongoing hormonal and immunologic changes.[3][11][13] As pregnancy advances, natural immunosuppression leads to a decline in TRAb titers, particularly in the second half of gestation.[2][5][7][9] This immunologic shift often translates into reduced autoimmune stimulation of the thyroid and may permit gradual reduction of ATD doses. TRAb levels can be remeasured in the third trimester, and if titers are low or undetectable, clinicians may consider tapering or even discontinuing ATDs, provided maternal thyroid function remains within target ranges.[2][3][9][11] This strategy minimizes fetal exposure to ATDs while leveraging the protective effect of pregnancy-associated immune modulation. Adverse effects of thioamide therapy are not uncommon, occurring in up to 15% of women, but the majority are mild and self-limited.[1][3] The most frequent complaints are pruritic rash and generalized itching, which can often be managed symptomatically or by switching from one ATD to the other if necessary.[1][3] Other reported side effects include arthralgias, low-grade fever, gastrointestinal upset such as nausea, and alterations in taste.[1][9] Serious complications, although rare, must be promptly recognized and managed. These include agranulocytosis, which can present with fever and sore throat; antineutrophil cytoplasmic antibody–associated vasculitis; severe sepsis; and hepatotoxicity, particularly with PTU.[1][9] Patients should be counseled to seek immediate medical attention if they develop symptoms suggestive of infection or liver dysfunction, such as jaundice, dark urine, or significant right upper quadrant pain.

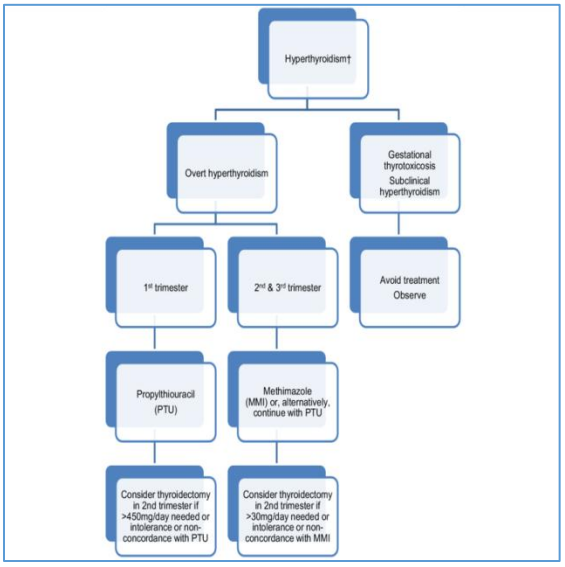

Figure-2: Management of Thyroid disorders in pregnancy.

Alternative or adjunctive pharmacologic approaches may be considered in selected cases. Potassium iodide (KI) has been used as a treatment for mild hyperthyroidism, primarily in Japan, where dietary iodine intake is relatively high.[2][9][12] Limited observational data suggest that KI can be effective in achieving biochemical control with minimal adverse fetal effects in this context.[2][9][12] However, extrapolation to populations with lower iodine intake is uncertain, and concerns remain that excessive iodine exposure could exacerbate or induce hypothyroidism in susceptible fetuses. Accordingly, KI may be considered only for women with mild disease who are unable to tolerate ATDs, and its use requires close endocrine and obstetric supervision.[2][9][12] Surgical management, usually by total or near-total thyroidectomy, is reserved for situations in which medical therapy is insufficient, contraindicated, or poorly tolerated. Indications include failure to achieve adequate control with high doses of ATDs, severe allergic reactions or life-threatening adverse effects from ATDs, or the presence of a large goiter causing compressive symptoms such as dysphagia or airway compromise.[2][3][5][11] When surgery is deemed necessary during pregnancy, the second trimester is generally considered the safest window, as the risk of miscarriage is higher in the first trimester and the risk of preterm labor and other complications increases in the third.[2][3][5][11] Preoperative optimization with beta-blockers and, when feasible, short-term ATD therapy is recommended to reduce the risk of thyroid storm. After thyroidectomy, levothyroxine replacement is initiated and adjusted to maintain maternal euthyroidism. A particularly complex scenario arises in women with Graves' disease who were treated before pregnancy with thyroidectomy or radioiodine ablation. In such patients, maternal thyroid function is typically maintained with levothyroxine; however, TRAbs may persist for years and continue to cross the placenta, placing the fetus at risk of hyperthyroidism even when the mother is biochemically euthyroid or hypothyroid.[1][9][12] In these cases, a "block-and-replace" strategy may be employed. This approach involves administering ATDs to control fetal hyperthyroidism—since ATDs readily cross the placenta—while simultaneously providing sufficient levothyroxine to

maintain maternal euthyroidism, as levothyroxine crosses the placenta less efficiently.[5][9][12] Such management requires close collaboration between endocrinology, maternal–fetal medicine, and neonatology, with careful adjustment of drug doses based on maternal thyroid function, TRAb titers, and fetal surveillance findings.

Radioiodine ablation (RAI), a definitive treatment option for hyperthyroidism outside of pregnancy, is absolutely contraindicated during pregnancy. Radioiodine crosses the placenta and can concentrate in the developing fetal thyroid gland once it becomes functional, leading to thyroid ablation and permanent congenital hypothyroidism if administered after fetal thyroidal uptake begins.[3][5][8][13] Even earlier in gestation, before the fetal thyroid is functional, exposure to RAI may increase the risk of spontaneous miscarriage or congenital malformations.[3][5][8][13] For women of reproductive age who elect RAI outside pregnancy, current recommendations advise deferring conception for at least six months after treatment to ensure complete clearance of radioiodine and to allow time for stabilization of maternal thyroid status on levothyroxine replacement.[3][5][8][13] Symptomatic management with beta-adrenergic blockers, such as propranolol, can be very useful in controlling adrenergic manifestations of hyperthyroidism, including palpitations, tremor, and anxiety, especially early in the course of treatment or around the time of dose adjustments.[1][2][5] These agents provide rapid symptomatic relief while ATDs, which act at the level of hormone synthesis, take several weeks to exert their full effect. Once a stable euthyroid state is achieved, beta-blockers should be tapered and discontinued because prolonged use has been associated with adverse fetal outcomes, including intrauterine growth restriction, fetal bradycardia, and neonatal hypoglycemia.[2][3][9][16] As with all aspects of therapy in pregnant patients, the duration and dose of beta-blockers should be kept as low as feasible and tailored to symptom severity. Throughout treatment and management, nursing and multidisciplinary care are critical. Nurses play a central role in medication education, adherence support, recognition of early signs of adverse drug reactions, and coordination of frequent laboratory monitoring and clinic visits. Education regarding warning symptoms of agranulocytosis, hepatotoxicity, or decompensated thyrotoxicosis equips pregnant patients to seek timely care and enhances overall safety. Close collaboration among obstetricians, endocrinologists, anesthesiologists, and neonatologists ensures individualized planning for labor, delivery, and postpartum follow-up, which is particularly important given the risk of postpartum relapse in autoimmune thyroid disease.[2][10]

Fetal Surveillance

Effective management of hyperthyroidism in pregnancy extends beyond maternal treatment to include vigilant fetal surveillance, particularly in women with Graves' disease or elevated TRAb titers. The fetal thyroid gland begins to develop function around 12 weeks of gestation, but fetal thyroxine production does not reach physiologically sufficient levels until approximately 18 to 20 weeks.[17] Prior to this time, the fetus is heavily dependent on maternal thyroid hormone transferred across the placenta, and maternal thyroid status therefore has a direct influence on early fetal neurodevelopment.[17] For pregnant women with current or past Graves' disease, the routine fetal anatomy ultrasound, typically performed between 18 and 22 weeks of gestation, offers an important opportunity to assess the fetal thyroid and screen for indirect signs of thyroid dysfunction.[3][9][11][13] During this detailed survey, the sonographer should evaluate for fetal goiter, which may appear as a symmetric enlargement of the anterior neck, as well as more systemic manifestations of thyroid imbalance. Ultrasound and Doppler findings that may suggest fetal hyper- or hypothyroidism include intrauterine growth restriction, hydrops fetalis, advanced bone maturation, persistent fetal tachycardia, cardiac failure, oligohydramnios, and changes in fetal activity.[3][9][11][13] Fetal tachycardia, often defined as a sustained heart rate above 160 beats per minute, is particularly characteristic of fetal hyperthyroidism, whereas bradycardia may point toward hypothyroidism, especially in the context of goiter. Because TRAbs can cross the placenta and directly stimulate or inhibit the fetal thyroid, serial measurement of maternal TRAb levels is an important component of risk stratification. It is recommended that TRAbs be remeasured between 18 and 22 weeks and again between 30 and 34 weeks of gestation to evaluate the ongoing risk of fetal and neonatal hyperthyroidism, respectively.[2][5] Persistently elevated or rising titers, particularly those exceeding three times the upper limit of normal, are associated with an increased likelihood of fetal thyroid dysfunction and warrant intensified fetal monitoring.[3] A prior history of a neonate with Graves' disease or other thyroid disorder also heightens concern and justifies a more aggressive surveillance strategy.[3]

Enhanced fetal surveillance may include serial growth ultrasounds to assess for appropriate somatic development and to detect early evidence of growth restriction.[3][5][11] Amniotic fluid volume measurements can be informative, as both polyhydramnios and oligohydramnios may accompany significant fetal disease. Regular evaluation of fetal heart rate, either via ultrasound or nonstress testing later in gestation, can help identify persistent tachycardia or bradycardia suggestive of thyroid dysfunction.[3][5][11] In some cases, specific fetal thyroid ultrasound with targeted assessment for goiter and vascularity may provide additional diagnostic clues; for example, a highly vascular goiter may support a diagnosis of hyperthyroidism, whereas a poorly vascular goiter may be more consistent with hypothyroidism secondary to overtreatment with ATDs.[3][5][11] The information gathered from fetal surveillance directly informs therapeutic decisions. If evidence of fetal hyperthyroidism emerges in the setting of elevated TRAbs and maternal euthyroidism or mild hyperthyroidism, clinicians may elect to increase maternal ATD dose to suppress excessive fetal thyroid hormone production.[2][3][5][11] Conversely, signs of fetal hypothyroidism—such as growth restriction, reduced heart rate, or a characteristic pattern of goiter—may prompt a reduction in maternal ATD dose, especially if maternal free T4 is at the low end of the normal range.[2][3][5][11] These adjustments require careful balancing to protect the fetus while maintaining maternal euthyroidism, and close follow-up is essential to assess response. In summary, treatment and management of hyperthyroidism in pregnancy demand an integrated approach that simultaneously addresses maternal hormonal control, drug safety, and fetal well-being. Judicious use of ATDs, timely switching from PTU to methimazole, appropriate laboratory monitoring, consideration of surgical options when indicated, and strict avoidance of radioiodine

therapy form the foundation of maternal care.[2][3][5][8][11][13][15][16] Parallel to these measures, structured fetal surveillance—guided by gestational age, TRAb titers, and ultrasound findings—enables early detection and targeted intervention for fetal thyroid dysfunction.[2][3][5][9][11][13][17] Through close multidisciplinary collaboration and individualized risk assessment, clinicians can optimize outcomes for both mother and child in the challenging context of hyperthyroidism during pregnancy.

Differential Diagnosis

The differential diagnosis of hyperthyroidism in pregnancy is broad and requires careful clinical and biochemical assessment to distinguish pathological causes from physiological adaptations of gestation. While Graves' disease remains the leading cause of clinically significant hyperthyroidism in pregnancy, it is essential to consider alternative etiologies, as management strategies and the need for antithyroid therapy differ substantially among them.[9] Accurate differentiation helps avoid unnecessary treatment in self-limited conditions and ensures targeted intervention in disorders that pose significant maternal and fetal risk. Gestational transient thyrotoxicosis (GTT), also termed transient gestational hyperthyroidism (TGH), is the most common cause of transient hyperthyroidism in pregnancy and is reported to affect approximately 1% to 3% of pregnancies, making it more frequently encountered than Graves' disease in this setting.[2][5][7][11] GTT arises from the structural homology between the beta subunit of human chorionic gonadotropin (hCG) and thyroid-stimulating hormone (TSH), which allows hCG to weakly stimulate the TSH receptor. During the first trimester, rapidly rising hCG levels result in increased secretion of free T4, total T4, and total T3, with a corresponding decrease in TSH.[2][3][5][17] This form of hyperthyroidism is typically mild and self-limited, resolving spontaneously by about 14 to 20 weeks' gestation as hCG concentrations fall, and it generally does not require treatment with antithyroid drugs.[2][3][5][17] Clinically, GTT is often associated with significant nausea and vomiting, sometimes severe enough to meet criteria for hyperemesis gravidarum, and up to 50% to 70% of women with hyperemesis gravidarum may demonstrate biochemical hyperthyroidism.[1][3][7] GTT can be distinguished from Graves' disease by the absence of TRAbs, lack of goiter and ophthalmopathy on examination, and a normal thyroid texture on ultrasound.[2][7] The risk of GTT increases in conditions with markedly elevated hCG levels, such as multifetal gestations and molar pregnancies, where hCG levels frequently exceed 200,000 IU/L.[2][5][7]

Hydatidiform molar pregnancies, a subset of gestational trophoblastic disease, represent another important cause of hyperthyroidism in pregnancy. Complete molar pregnancies are especially associated with extremely high hCG levels, which may drive excessive stimulation of TSH receptors and result in clinically significant thyrotoxicosis.[9] In such cases, definitive management requires evacuation of the molar tissue, typically via dilation and suction curettage, after which thyroid function often normalizes as hCG levels decline.[8] Other causes of hyperthyroidism include single toxic adenoma and toxic multinodular goiter, both of which involve autonomously functioning thyroid nodules producing excess thyroid hormone independent of TSH regulation.[2][7] These entities are more commonly observed in women aged 40 years or older and are therefore less frequent in typical pregnant populations.[2][7] The magnitude of hormone production from these nodules is usually lower than that seen in Graves' disease, and symptoms may be milder. Consequently, antithyroid drugs may not always be required, and when used, they carry a proportionally greater risk of inducing fetal hypothyroidism because there are no competing stimulatory TRAbs driving fetal thyroid activity.[5] Thyroid ultrasound can assist by demonstrating nodularity, but definitive diagnosis often relies on thyroid scintigraphy, a functional imaging modality that is absolutely contraindicated in pregnancy due to radiation exposure.[5] Subacute thyroiditis, or DeQuervain subacute thyroiditis, represents a rare inflammatory cause of hyperthyroidism, typically triggered by a viral infection and characterized by painful thyroid enlargement and transient release of preformed thyroid hormone.[9] Although uncommon in pregnancy, it should be considered in women with neck pain, elevated inflammatory markers, and a hyperthyroid biochemical profile but low radioiodine uptake outside of pregnancy.

Genetic and receptor-level abnormalities also contribute to the differential diagnosis. Mutations in the thyroid hormone receptor may result in resistance to thyroid hormone, a condition characterized by elevated thyroid hormone levels with inappropriately normal or elevated TSH.[9] In pregnancy, this can lead to excessive fetal exposure to thyroid hormone and an increased risk of spontaneous abortion.[9] Additionally, activating mutations of the TSH receptor can cause hyperresponsiveness to hCG, producing a hyperthyroid state similar to gestational transient thyrotoxicosis.[2][3][9] These rare conditions require specialized endocrine evaluation and may be suspected when clinical and biochemical findings are discordant or when there is a strong family history. Neoplastic causes, though rare, should not be overlooked. Struma ovarii is an ovarian teratoma composed predominantly of functional thyroid tissue and can present as hyperthyroidism in pregnancy when the ectopic thyroid tissue secretes sufficient hormone.[1][9] Diagnosis typically involves pelvic imaging and, in nonpregnant individuals, radionuclide scanning demonstrating uptake in the ovary rather than the cervical thyroid. A TSH-producing pituitary adenoma represents another rare source of hyperthyroidism, characterized by elevated or inappropriately normal TSH levels with high circulating thyroid hormones.[9] Management usually involves neurosurgical and endocrinologic input. In patients with differentiated thyroid carcinoma, metastatic deposits may, in rare cases, retain the ability to synthesize thyroid hormone and thus contribute to hyperthyroidism.[9]

Iatrogenic causes must also be considered, particularly excessive intake of levothyroxine prescribed for hypothyroidism.[11] Over-replacement can lead to biochemical and clinical hyperthyroidism, which may be misinterpreted as endogenous disease. In pregnant women already receiving levothyroxine, dose adjustments are common due to increased physiological demands, and careful titration is necessary to avoid both under- and over-treatment.[11] In summary, the differential diagnosis of hyperthyroidism in pregnancy encompasses a spectrum ranging from physiologic or transient conditions such as GTT to autoimmune, structural, genetic, neoplastic, and

iatrogenic causes.[1][2][3][5][7][8][9][11][17] Distinguishing among these entities using a combination of clinical history, physical examination, targeted laboratory evaluation—including TRAbs and TSH patterns—and imaging where safe is vital for guiding appropriate treatment decisions and optimizing outcomes for both mother and fetus.

Prognosis

The prognosis of hyperthyroidism in pregnancy depends largely on the timeliness of diagnosis, adequacy of treatment, and rigor of ongoing laboratory monitoring. With appropriate antithyroid therapy and close observation of thyroid function tests, maternal and fetal outcomes improve substantially, and the incidence of serious complications is significantly reduced.[3][9][10][11] Pregnant individuals remain at the highest risk when overall control of hyperthyroidism is poor, either because of delayed diagnosis, suboptimal medication dosing, poor adherence, or coexisting medical conditions. In the absence of treatment, sustained thyrotoxicosis imposes a considerable hemodynamic burden, and up to 10% of patients may develop congestive heart failure, particularly those with preexisting cardiac disease or severe, long-standing hyperthyroidism.[1] Thyroid storm, the most extreme manifestation of decompensated thyrotoxicosis, is life-threatening and complicates approximately 1% to 2% of hyperthyroid pregnancies, with high rates of morbidity and mortality if not promptly recognized and aggressively managed.[3] Many pregnant individuals with Graves' disease experience partial remission of hyperthyroidism toward the later stages of gestation. This improvement results from the immunosuppressive milieu of pregnancy, which diminishes autoimmune activity and reduces TRAb titers.[12] In some cases, there may even be a functional shift in TRAb populations, with stimulating antibodies declining and, occasionally, inhibitory antibodies becoming more prominent, further attenuating thyroid hormone overproduction.[12][16] As a result, antithyroid drug requirements often decrease in the second and third trimesters, and some women may be able to taper or discontinue therapy under careful supervision.[3][9][11]

The postpartum period, however, is characterized by reactivation of the immune system, and this rebound is associated with a high risk of exacerbation or relapse of Graves' disease. The risk of relapse is greatest between 7 and 9 months postpartum, although it can occur anytime between 3 and 18 months after delivery.[5][11][12] Most individuals who were in apparent remission before pregnancy will either relapse postpartum or experience some form of thyroid dysfunction, including postpartum thyroiditis.[1] From a fetal standpoint, thyroid hormones are fundamental to normal neurocognitive development and somatic growth, particularly in early gestation when the fetus relies heavily on maternal hormone supply. Inadequately treated maternal hyperthyroidism has been associated with preeclampsia, preterm birth, intrauterine growth restriction, and fetal hyperthyroidism, each of which carries short- and long-term consequences for child health.[4] Nevertheless, when maternal thyroid function is carefully controlled and fetal surveillance is appropriately targeted, most pregnancies in women with hyperthyroidism can result in favorable outcomes for both mother and child.[3][9][10][11]

Complications

The spectrum of complications associated with hyperthyroidism in pregnancy includes both maternal and fetal consequences and underscores the importance of prompt recognition and effective treatment. For the mother, persistent overt thyrotoxicosis is linked to a higher incidence of pregnancy loss, including spontaneous abortion and intrauterine fetal demise.[2][3][5][14] Hyperthyroidism is also associated with gestational hypertension and preeclampsia, likely mediated through hemodynamic stress, endothelial dysfunction, and metabolic derangements.[2][3][5] The risk of placental abruption and preterm labor is increased in women whose thyroid disease remains inadequately controlled, reflecting the impact of systemic hypermetabolism on uteroplacental circulation and uterine contractility.[2][3][5][14] Among the most severe maternal complications is thyroid storm, in which uncontrolled hyperthyroidism progresses to acute decompensation. In this setting, women are at heightened risk of congestive heart failure, intensive care unit admission, and maternal death despite modern supportive care.[2][3][5][14] Evidence suggests that appropriate diagnosis and management of thyroid dysfunction may reduce the maternal risk of preeclampsia and other hypertensive complications, further underscoring the importance of vigilant monitoring.[18] Adequate levels of thyroid hormones are equally critical for fetal growth and development. Thyroid hormones regulate key aspects of brain morphology, including neuronal proliferation, migration, synaptogenesis, and myelination; disturbances in maternal or fetal thyroid status during critical developmental windows can therefore have lasting neurocognitive consequences.[3] Fetal complications associated with uncontrolled maternal hyperthyroidism include prematurity, low birth weight, fetal goiter, persistent tachycardia, heart failure, fetal hydrops, and early ossification with advanced bone maturation.[2][5][13][15] Intrauterine growth restriction and neurodevelopmental abnormalities have also been reported, alongside a higher risk of structural congenital anomalies. Many of these effects are mediated through the transplacental transfer of excess maternal thyroid hormone or TRAbs, which stimulate the fetal thyroid and drive intrauterine thyrotoxicosis.[2][5][13][15] The likelihood and severity of fetal effects increase in proportion to maternal TRAb concentrations, making TRAb measurement a critical component of risk stratification and surveillance.[2] Overtreatment of maternal hyperthyroidism with ATDs poses a distinct set of risks. Excessive dosing can suppress both maternal and fetal thyroid function, resulting in fetal hypothyroidism, which may manifest as goiter, growth restriction, and delayed skeletal maturation.[2][5][13] Conversely, women who receive carefully titrated antithyroid treatment during pregnancy generally deliver euthyroid neonates. However, TRAbs that crossed the placenta before birth remain in the neonatal circulation, even after ATDs are rapidly metabolized by the infant within 2 to 3 days of delivery.[2][5][9][11] As a result, some newborns develop neonatal hyperthyroidism, which occurs in approximately 1.5% to 2% of infants born to mothers with Graves' disease.[2][5][9][11] This condition may resolve spontaneously within several weeks as maternal antibodies are cleared or may persist for 4 to 6 months. Persistent neonatal hyperthyroidism is associated with a reported 27% morbidity and 1.2% mortality, with potential sequelae including heart failure, hepatic dysfunction, microcephaly, craniosynostosis, pulmonary

hypertension, coagulopathy, and intellectual disability.[11] Early recognition, close monitoring, and timely intervention are therefore critical to improving outcomes in affected neonates.

Thyroid Storm

Thyroid storm represents the most severe, life-threatening complication of hyperthyroidism and is characterized by an extreme, decompensated state of thyrotoxicosis. In pregnancy, this condition is particularly dangerous because it threatens the well-being of both mother and fetus. Thyroid storm typically arises in individuals with poorly controlled or undiagnosed hyperthyroidism and is often precipitated by an acute stressor. Common triggers include labor and delivery, cesarean section, preeclampsia, trauma, major surgery, hypoglycemia, diabetic ketoacidosis, or systemic infections.[2][3][9][19] These events amplify the metabolic and cardiovascular stress imposed by excess thyroid hormone, precipitating a rapid clinical decline. Clinically, patients with thyroid storm present with severe tachycardia or tachyarrhythmias, often out of proportion to the degree of fever or other symptoms. Additional manifestations include marked heat intolerance, high-grade fever, profuse diaphoresis, agitation, confusion or frank delirium, nausea, vomiting, diarrhea, and sometimes abdominal pain.[2][3][9][19] Cardiovascular compromise may progress to congestive heart failure and hypotension, while multisystem involvement can culminate in hepatic dysfunction, coagulopathy, and multiorgan failure. The diagnosis is largely clinical, as laboratory values of thyroid hormones may not be dramatically higher than in uncomplicated hyperthyroidism; it is the severity of systemic manifestations that distinguishes thyroid storm from less severe thyrotoxicosis.[2][3][9][19]

Management of thyroid storm requires immediate intensive care and a multifaceted therapeutic strategy. In addition to high-dose ATDs such as PTU or methimazole to inhibit new hormone synthesis, aggressive supportive care is paramount, including intravenous fluid resuscitation, electrolyte correction, external cooling, and supplemental oxygen.[2][3][9][19] PTU has the theoretical advantage of also inhibiting peripheral conversion of T4 to T3, although either PTU or methimazole may be used depending on clinical circumstances and local protocols. At least one hour after initiating ATD therapy, potassium iodide or Lugol solution is administered to block further release of preformed thyroid hormone from the gland; if given before or too soon after ATDs, iodide can paradoxically worsen hormone synthesis and exacerbate the storm.[2][3][9][19] Beta-blockers, such as propranolol, are used to control tachycardia and arrhythmias and to reduce adrenergic symptoms. High-dose glucocorticoids not only support adrenal function but also decrease peripheral T4-to-T3 conversion, contributing to more rapid hemodynamic stabilization. In the presence of heart failure, digoxin may be used cautiously to improve cardiac output, though its efficacy can be reduced in hyperthyroid states. Equally important is identification and treatment of the precipitating event. For example, broad-spectrum antibiotics are indicated when infection is suspected, and other triggers, such as ketoacidosis or preeclampsia, require disease-specific interventions.[2][3][9][19] Antipyretic management should employ acetaminophen rather than aspirin, as salicylates can displace thyroid hormones from binding proteins and raise free hormone levels, thereby aggravating thyrotoxicosis.[3][9][19] Fetal monitoring is essential, as fetal distress is frequently present at initial presentation; reassuringly, fetal status often improves as maternal hemodynamics stabilize. Delivery should generally be avoided during the acute phase, as both labor and cesarean section can exacerbate the storm. Once the maternal condition is stabilized, delivery planning can proceed with multidisciplinary input, balancing obstetric indications and maternal endocrine status.[3]

Postpartum Thyroiditis

Postpartum thyroiditis (PPT) is an autoimmune-mediated thyroid dysfunction that arises after delivery and reflects the rebound of immune activity following the relative immunosuppression of pregnancy. PPT typically occurs within 6 weeks postpartum but can develop anytime within the first year after birth, with this extended window reflecting the variable timing of immune reconstitution.[8][9] The condition is characterized by the presence of antithyroid peroxidase (TPO) antibodies, whereas TRAbs are usually absent, helping to distinguish PPT from postpartum Graves' disease.[8] Clinically, PPT often follows a biphasic or triphasic course. The initial phase is typically one of transient hyperthyroidism, resulting from autoimmune destruction of thyroid follicular cells and subsequent leakage of preformed thyroid hormones into the circulation.[8][9] This destructive thyrotoxicosis may manifest with palpitations, heat intolerance, anxiety, and fatigue, although symptoms can be subtle and may be mistaken for normal postpartum changes or postpartum mood disorders. Because PPT results from hormone leakage rather than increased synthesis, radioiodine uptake (outside pregnancy and lactation) is low, and ATDs are ineffective in altering the course of disease.[8][9] As the stores of preformed hormone become depleted, many women enter a hypothyroid phase marked by fatigue, cold intolerance, weight gain, constipation, and depressive symptoms, which can significantly affect maternal quality of life and caregiving capacity.[8][9] This hypothyroid phase may resolve spontaneously, but in some women it persists and evolves into permanent hypothyroidism requiring long-term levothyroxine therapy.[8][9] Differentiating PPT from new-onset Graves' disease is crucial because the management strategies differ substantially. In PPT, the hyperthyroid phase is transient and generally does not require ATDs, as the underlying mechanism is inflammatory destruction rather than increased hormone synthesis.[8][9] Symptomatic management with beta-blockers may be used for short periods to control palpitations, tremor, and anxiety, particularly in breastfeeding mothers, with careful attention to neonatal monitoring.[8][9] In contrast, Graves' disease typically requires ATDs and is associated with positive TRAbs, goiter, and possibly ophthalmopathy. The overall incidence of PPT is approximately 5.4%, making it a relatively common postpartum endocrine disorder.[8] Women with type 1 diabetes mellitus are at particularly high risk, with a three- to fourfold increase compared with the general population, likely due to shared autoimmune mechanisms.[8] Early recognition and appropriate counseling about the natural history of PPT, along with timely initiation of levothyroxine in the hypothyroid phase when indicated, can substantially improve maternal well-being and support optimal infant care.

Deterrence and Patient Education

Deterrence of adverse outcomes associated with hyperthyroidism in pregnancy begins with comprehensive patient education and preconception counseling. Women with known Graves' disease who are planning a pregnancy should be counseled about available treatment options and the implications of each for maternal and fetal health.[2][5][8][14] For some, definitive therapy with surgery or RAI may be attractive before conception, especially in those with very high TRAb titers or a history of fetal or neonatal thyroid dysfunction in a prior pregnancy.[11] Thyroidectomy offers rapid control of hyperthyroidism without exposing future pregnancies to ATDs, but it requires lifelong levothyroxine replacement and carries surgical risks. RAI is another definitive option; however, in women with especially high TRAb titers, surgery may be preferred because RAI can initially increase TRAb concentrations, potentially exacerbating autoimmune activity.[2][8] Patient education should emphasize that achieving stable euthyroidism with levothyroxine before conception is essential for optimizing pregnancy outcomes and minimizing early embryonic risks.[8] Even after definitive therapy, women must understand that TRAbs may persist and cross the placenta in future pregnancies, potentially causing fetal hyperthyroidism. In such scenarios, a block-and-replace strategy, using ATDs to protect the fetus while maintaining maternal euthyroidism with levothyroxine, may be necessary and requires close monitoring.[5][9][12] For nonpregnant women with Graves' disease managed medically, methimazole is generally preferred due to its lower risk of severe hepatotoxicity relative to PTU.[9] Nonetheless, some women may opt to switch to PTU before conception, particularly if pregnancy is imminent, to limit first-trimester exposure to methimazole and its associated embryopathy. When women choose to remain on methimazole while attempting to conceive, it is vital to inform them about the increased risk of methimazole embryopathy if the medication is continued beyond conception and through organogenesis.[3][5][8][14] Thorough counseling should underscore the importance of early pregnancy recognition and prompt switching to PTU, ideally by the fifth week of gestation, to minimize teratogenic risk. When weighing teratogenic concerns against maternal safety, patients should be informed that, in this specific context, the risk of PTU-induced hepatotoxicity is considered lower than the risk of methimazole-associated congenital anomalies.[11] Clear communication, shared decision-making, and individualized risk assessment empower women to make informed choices regarding their treatment and timing of pregnancy, thereby enhancing both maternal and fetal outcomes.

Pearls and Other Issues

A key clinical pearl in the management of thyroid disease in pregnancy is that subclinical hyperthyroidism—defined by suppressed TSH with normal free T4 and T3 levels—is typically not associated with adverse maternal or fetal outcomes and thus does not require treatment.[2][5][10][12] Initiating ATD therapy in such cases can be more harmful than beneficial, as overtreatment may induce fetal hypothyroidism and related complications.[13] To avoid misdiagnosis and unnecessary therapy, clinicians must use correct trimester-specific reference ranges for TSH and interpret free T4 values in the context of pregnancy-induced changes in TBG and assay performance.[7] Accurate interpretation minimizes both under- and over-treatment, thereby preventing preventable complications. Another important consideration is the compatibility of ATDs with breastfeeding. Breastfeeding is not contraindicated in women taking low to moderate doses of ATDs. Patients should be advised to take their ATD dose immediately after breastfeeding to allow partial drug metabolism before the next feeding, thereby reducing neonatal exposure.[5] When higher ATD doses are required, monitoring neonatal free T4 is prudent to ensure that the infant remains euthyroid.[5] PTU crosses into breast milk to a lesser extent than methimazole, which historically made it attractive for lactating women. However, given the risk of serious maternal hepatotoxicity with PTU, current guidance generally favors methimazole during lactation, balancing maternal safety with acceptable neonatal exposure.[8][9][11] Radioiodine ablation is absolutely contraindicated in breastfeeding women. I-131 not only passes into breast milk but also concentrates in breast tissue, exposing both mother and infant to unnecessary radiation and risking damage to both maternal breast tissue and the infant's thyroid.[5][8][9] Therefore, breastfeeding must be discontinued well before any planned RAI therapy, and alternative strategies should be considered in women who wish to continue lactation. These practical considerations underscore the importance of tailoring therapy to the unique physiologic context of pregnancy and the postpartum period, with careful attention to both maternal and neonatal safety.[5][8][9]

Enhancing Healthcare Team Outcomes

Optimizing outcomes for pregnant women with hyperthyroidism requires coordinated efforts from an interprofessional healthcare team that includes obstetricians, endocrinologists, primary care clinicians, nurses, anesthesiologists, and neonatologists. Hyperthyroidism in pregnancy, although relatively rare, is characterized by elevated T4 and T3 levels with suppressed TSH, and prompt recognition is key to preventing serious complications for both mother and fetus. While achieving euthyroidism before conception is ideal, the reality of unplanned pregnancies underscores the importance of early detection during prenatal care. Early diagnosis and appropriate management can significantly reduce the risks of miscarriage, preeclampsia, preterm birth, and fetal thyroid dysfunction. The question of universal screening for thyroid disease in pregnancy remains controversial. Some professional organizations advocate targeted screening for high-risk individuals—such as those with a history of thyroid disease, type 1 diabetes, or other autoimmune disorders—whereas others argue for universal screening given the low cost of thyroid function tests and the potential to detect both overt and subclinical disease earlier.[7][10] Proponents of universal screening suggest that testing all pregnant women at the initial prenatal visit would facilitate earlier diagnosis and treatment, potentially improving maternal and fetal outcomes. Preconception screening for thyroid disease is another option, although there is currently no consensus, and further research is needed to clarify its cost-effectiveness and impact on long-term outcomes.[14]

In settings without universal screening, it is crucial that all members of the healthcare team remain vigilant for symptoms of hyperthyroidism during

pregnancy. Clinicians, nurses, and medical assistants should be trained to elicit a thorough history that includes known thyroid disease, previous thyroid surgery or RAI, current or past use of ATDs, and any complications in prior pregnancies related to thyroid dysfunction.[13] Primary care providers and endocrinologists should routinely ask women with Graves' disease about their pregnancy plans so that thyroid hormone levels can be optimized and appropriate counseling provided before conception.[2][12][14] Patients should be advised to delay conception until they are euthyroid and stable on therapy, minimizing risks associated with uncontrolled disease early in pregnancy. Antithyroid medication regimens should ideally be adjusted by approximately 5 weeks of gestation to reduce inappropriate fetal exposure and to ensure that maternal thyroid hormone levels are appropriately targeted from the earliest stages of organogenesis.[12] Communication between obstetric and endocrine teams is essential for coordinating dose changes, laboratory monitoring, and fetal surveillance. Neonatologists should be informed in advance of deliveries involving women with Graves' disease so they can promptly evaluate newborns for signs of transient hyperthyroidism or neonatal Graves' disease due to transplacental TRAbs.[3][11] Early recognition and treatment of neonatal thyroid dysfunction are vital to preventing serious complications and supporting healthy neurodevelopment. In this way, a coordinated, team-based approach that emphasizes early recognition, evidence-based management, and careful perinatal planning can significantly enhance outcomes for both mother and baby.

Conclusion:

In conclusion, the effective management of hyperthyroidism during pregnancy is paramount for ensuring the well-being of both the mother and the fetus. While the condition presents diagnostic challenges due to overlapping symptoms with normal pregnancy, a systematic approach involving trimester-specific thyroid function testing and thyrotropin receptor antibody (TRAb) measurement allows for accurate diagnosis and risk stratification. The cornerstone of treatment remains antithyroid drug (ATD) therapy, with a carefully considered strategy of using Propylthiouracil (PTU) during the first trimester to minimize the risk of methimazole embryopathy, followed by a transition to Methimazole (MMI) for the remainder of the pregnancy to reduce the potential for PTU-induced hepatotoxicity. The primary goal is to maintain maternal free thyroxine at the high end of the normal range using the lowest possible ATD dose, thereby preventing both maternal thyrotoxicosis and fetal hypothyroidism. Crucially, management extends beyond maternal biochemical control to include dedicated fetal surveillance. In women with Graves' disease or positive TRAbs, serial ultrasounds to assess for goiter, growth, and tachycardia are essential to detect and manage fetal thyroid dysfunction. A coordinated, interprofessional team involving endocrinologists, obstetricians, and neonatologists is vital for optimizing outcomes. Through vigilant monitoring, judicious medication use, and comprehensive patient education, the significant risks associated with hyperthyroidism in pregnancy—such as preeclampsia, preterm birth, and fetal thyrotoxicosis—can be substantially mitigated, leading to successful maternal and neonatal outcomes.

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