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Hyperthyroidism Management in Saudi Arabia: Current Practices, Challenges, and Future Directions

—A Multidisciplinary Approach to Diagnosis, Treatment, and Long-Term Care

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Abstract

In Saudi Arabia, the management of hyperthyroidism is influenced by several factors: genetic, environmental, and the healthcare system. Thus, a tailored approach is mandatory. A region-specific consensus is highly needed because of variations in clinical practice. A multidisciplinary expert team of endocrinologists and internal medicine experts convened to coin a local consensus on the care of hyperthyroidism. The expert meeting assessed current management methods, identified critical challenges, and provided evidence-based recommendations. The current article is the culmination of a consensus that developed through a structured, multi-phase process involving a systematic literature review, a pre-meeting survey, and expert panel discussions to assess the topic comprehensively. A literature review of databases such as PubMed and the Saudi Digital Library, focusing on publications from 2010 to 2024, evaluated the evidence on diagnosis, management, and treatment strategies,

with priority given to regional guidelines, randomized controlled trials, and systematic reviews. A pre-meeting survey of medical experts revealed current practices, challenges, and unmet requirements, which informed expert discussions. The expert panel analyzed survey results and literature, then held structured discussions concerning illness burden, best practices, and gaps in care. The Delphi approach was employed to develop recommendations that ensured consensus and alignment with global standards, while also addressing region-specific issues. The finalized recommendations will be shared through conferences, seminars, and publications, with ongoing feedback to help develop and update the guidelines.

Keywords

Hyperthyroidism, Management, Saudi Arabia, Recommendations

1. Introduction

Hyperthyroidism is a common endocrine disorder characterized by excessive thyroid hormone production, leading to a range of systemic effects that significantly impact patients' health and quality of life. The management of hyperthyroidism requires a comprehensive approach, incorporating accurate diagnosis, risk stratification, and individualized treatment plans. In Saudi Arabia, the burden of hyperthyroidism is influenced by genetic, environmental, and healthcare system factors, necessitating a tailored approach to management [1] [2].

Despite established guidelines for hyperthyroidism treatment, variations in clinical practice exist, highlighting the need for a region-specific consensus. This expert meeting aims to assess the current management landscape of hyperthyroidism in Saudi Arabia, identify key challenges, and address unmet needs in medical therapy. Through a multidisciplinary discussion, this meeting will provide evidence-based recommendations to optimize patient outcomes, improve adherence to best practices, and enhance healthcare resource utilization. The task force, including endocrinologists and internal medicine experts, gathered to develop an explicit, evidence-based consensus on hyperthyroidism management in the Kingdom of Saudi Arabia (KSA). This article presents the recommendations of this expert panel.

2. Methodology

Consensus Development Process (Figure 1)**:** This consensus report is based on a structured, multi-phase process, including a literature review, a pre-meeting survey, and an expert panel discussion. This approach ensures a comprehensive assessment of current clinical practices, challenges, and opportunities for improving hyperthyroidism management in Saudi Arabia.

Systematic Literature Review: A systematic literature review was conducted to evaluate the current evidence on hyperthyroidism diagnosis, management, and

treatment strategies, with a specific focus on Saudi Arabia and the Middle East. Databases searched included PubMed, Scopus, and the Saudi Digital Library, covering publications from January 2010 to March 2024. The following search terms were applied using Boolean operators: ("hyperthyroidism" OR "thyrotoxicosis" OR "Graves' disease") AND ("Saudi Arabia" OR "Middle East") AND ("management" OR "treatment" OR "guidelines").

Inclusion criteria were: 1) peer-reviewed studies or national guidelines published in English or Arabic; 2) studies reporting on epidemiology, diagnosis, or management of hyperthyroidism; 3) human studies conducted in Saudi Arabia or Middle Eastern populations. **Exclusion criteria** were: 1) case reports with <5 patients; 2) animal or in vitro studies; 3) non-original articles such as commentaries or editorials unless they contained national recommendations; 4) duplicate publications.

From an initial 356 records identified across databases, 284 remained after duplicates were removed. Following title and abstract screening, 97 full-text articles were assessed for eligibility. Of these, 46 met the inclusion criteria and were included in the final synthesis (Figure 2). Local reports, national guidelines, and epidemiological studies were additionally reviewed to ensure a comprehensive overview of disease burden and clinical practices in the region.

Pre-meeting Survey: Before the expert panel meeting, a structured electronic survey was distributed to endocrinologists, internists, and general practitioners across Saudi Arabia through the Saudi Endocrine Society membership list and professional mailing groups (sampling frame ≈ 420 clinicians). A total of 168 responses were received (response rate 40%). Respondents represented all five major regions of Saudi Arabia (Central 34%, Western 28%, Eastern 20%, Northern 10%, Southern 8%). Clinician demographics included 67% endocrinologists, 22% internists, and 11% general practitioners, with a mean clinical experience of 14 ± 6 years (Table 1).

Table 1. Survey results.

Characteristic	n = 168 respondents
Specialty	Endocrinologists 67%; Internists 22%; GPs 11%
Clinical experience (years)	14 ± 6 years
Regional distribution	Central 34%; Western 28%; Eastern 20%; Northern 10%; Southern 8%
Most cited diagnostic challenges	• Delays in referral (75%) • Limited TRAb testing (25%) • Variability in ultrasound quality (31%) • Technetium scan (50%)
Most cited treatment barriers	• Limited radioiodine availability (47%) • Poor follow-up adherence (39%) • Access to newer antithyroid drugs (25%)
Top unmet needs identified	• National treatment protocols (62%) • Patient and PCP education programs (53%) • Better access to endocrinology care (48%)

The survey assessed diagnostic and treatment strategies, barriers to optimal care, challenges in guideline implementation, unmet needs, and areas for improvement. Table 1 presents the core survey findings, including the most frequently cited diagnostic challenges (limited access to TSH-receptor antibody testing, regional referral delays) and treatment barriers (radioiodine availability, follow-up adherence).

Delphi Consensus Process: A multidisciplinary expert panel convened to review the survey and literature findings. The Delphi method was used, consisting of three iterative rounds of anonymous voting and feedback. A ≥ 75% agreement threshold was required for consensus on each recommendation. Evidence was graded using a modified GRADE approach (high, moderate, low, very low). Items without consensus were revised and re-voted in subsequent rounds until alignment was achieved.

Adaptation to Local Context: International guidelines (e.g., American Thyroid Association, European Thyroid Association) were systematically reviewed and adapted to Saudi Arabia's specific context. Adjustments considered: A) Iodine status—accounting for historically borderline iodine sufficiency in certain regions. B) Healthcare access—variation in diagnostic resource availability (e.g., TRAb assays, nuclear medicine). C) Genetic/epidemiological factors—including higher prevalence of consanguinity-associated thyroid autoimmunity. This ensured recommendations were evidence-based yet clinically feasible in the Saudi healthcare system.

Expert Panel Meeting: The structured discussion focused on epidemiological trends, diagnosis and treatment, gaps in care, and practical recommendations. Panelists represented academic hospitals, Ministry of Health institutions, and private centers. Consensus statements were formulated, refined, and validated for clinical relevance and feasibility.

Dissemination Plan: The finalized recommendations will be disseminated through national conferences, workshops, webinars, and peer-reviewed publications. Targeted educational initiatives will support guideline adoption, with mechanisms for periodic updates based on new evidence.

Limitations: This consensus is limited by potential selection bias in the literature search and survey sampling, the relative scarcity of regional primary data, and the absence of formal cost-effectiveness analyses. Recommendations may evolve as new therapies and evidence emerge. A structured process for biennial updates has been planned to ensure continued relevance.

3. Epidemiology of Hyperthyroidism: Global, Regional, and Saudi Arabia

The global prevalence of hyperthyroidism is estimated at 0.2% - 2.5%. Overt hyperthyroidism, defined as suppressed thyrotropin (formerly thyroid-stimulating hormone) and elevated levels of triiodothyronine (T3) and/or free thyroxine (FT4), affects 0.2% to 1.4% of the global population. Graves' disease is the leading

cause of hyperthyroidism, with a global prevalence of 2% in women and 0.5% in males. Other causes of hyperthyroidism and thyrotoxicosis include toxic nodules and the thyrotoxic phase of thyroiditis. Subclinical hyperthyroidism, characterized as low thyrotropin and normal T3 and FT4 levels, affects 0.7% to 1.4% of the global population [3] [4].

Large-scale epidemiological studies are lacking in Saudi Arabia. However, the meta-analysis by Kargar *et al.* (2024) examined the prevalence of thyroid dysfunction disorders among adult populations in the Middle East, including Iran, Saudi Arabia, Egypt, Iraq, Turkey, and Jordan. The study found an overall pooled prevalence of thyroid disorders of 19.2%, with Saudi Arabia having the highest prevalence at 31.3%. Specifically, the prevalence of overt hyperthyroidism was 2.4%, and subclinical hyperthyroidism was 3.2%. The analysis revealed an increasing trend in thyroid disorders from 2000 to 2022, attributed to factors such as changing lifestyles, unhealthy diets, obesity, alcohol use, and smoking. The findings highlight the underappreciation of subclinical thyroid diseases, which can significantly impact patient management and treatment, suggesting a need for increased thyroid function screening and awareness among adults [5]-[7].

The high prevalence of thyroid disorders in Saudi Arabia may be linked to iodine deficiency and improper nutrition, as noted in previous studies. Variations in prevalence across Middle Eastern countries could be due to differences in study methodologies, environmental factors, iodination status, and diagnostic cut-off values. The study underscores the importance of addressing these disorders through improved screening, public health interventions, and awareness campaigns to mitigate the growing burden of thyroid dysfunction in the region [5]-[7].

The meta-analysis by Kargar *et al.* (2024), in Saudi Arabia, used data from 14 studies encompassing a total population of 18,520 individuals and indicates a high prevalence of thyroid dysfunction, affecting 31.3% (range: 17.9% - 54.9%). Among these, hypothyroidism was observed in 17.9% (10.5% - 30.3%), with subclinical hypothyroidism accounting for 18.9% (9.6% - 37.1%). Hyperthyroidism was less common, with overt hyperthyroidism affecting 4.0% (2.1% - 7.6%) and subclinical hyperthyroidism reported in 4.6% (1.7% - 11.8%) (**Figure 3**). These findings highlight a substantial burden of thyroid disorders in the region, emphasizing the need for effective screening and management strategies [5].

The prevalence of thyroid-related disorders varies by gender, age, geographical region, and dietary iodine consumption. Regional variations are obvious, with some regions having a higher frequency, most likely due to disparities in healthcare availability, dietary habits, and iodine intake. Rural locations encounter difficulties in early detection and screening [8]-[10].

Elmisbah *et al.* (2024), conducted a cross-sectional study between October 2023 and January 2024, enrolling 501 adults with diabetes in Arar, northern Saudi Arabia. The study found that 42.8% of participants had diabetes (mostly type 2), and 51.3% reported thyroid disorders. Vitamin D and B12 deficiencies were common

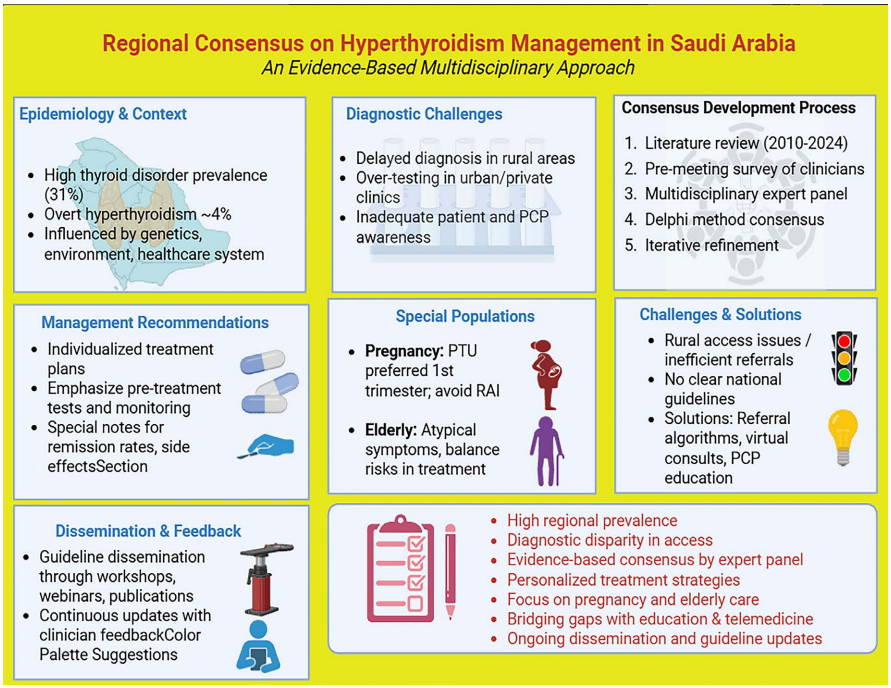

Figure 1. Graphical abstract.

comorbidities, along with hypertension and dyslipidemia. The authors concluded that thyroid disorders are highly prevalent among diabetics in the region, emphasizing the need for better awareness and early detection [11].

During the SARS-CoV2 (COVID) pandemic, there were reports of Graves' disease and subacute thyroiditis linked to COVID infection or vaccination, most likely due to COVID's immunogenic characteristics [12]-[14]. A retrospective analysis found that the prevalence of Graves' illness in a Spanish hospital increased twofold between 2020 and 2021 compared to the pre-COVID period of 2017 to 2019 [15].

4. Diagnostic Challenges

In the current study, common diagnostic tests for hyperthyroidism reveal varying practices among clinicians surveyed. All clinicians (100%) use free T3, free T4, and TSH as standard tests. A significant portion (75%) also test for thyroid receptor antibodies (TRAbs) and conduct full blood counts, while half (50%) perform technetium thyroid scans. These tests are essential for accurate diagnosis, but their utilization varies depending on clinical settings and resources.

Low serum TSH is the best test for detecting thyroid dysfunction, with a sensitivity of 92% - 95% and a specificity of 89% - 85%. Thyroid hormone can circulate as T3 or T4, which is a prohormone that is converted to T3 in peripheral tissues. T3 is a biologically active type of thyroid hormone. Free T4 levels can be used to determine the level of hyperthyroidism. T3 levels can also aid in determining the source and severity of thyrotoxicosis. Graves' disease or toxic nodules typically have a total T3:T4 ratio greater than 20:1, while thyroiditis has a ratio of less than

20:1 [16] [17].

Once thyrotoxicosis has been confirmed, the etiology should be determined. TSH-receptor antibodies (TRAbs) are pathognomonic for Graves' disease. Current guidelines advocate measuring TRAb as the first step in distinguishing Graves' illness from other types of thyrotoxicosis. There are two types of assays available for measuring TRAb [18]-[20].

The current study showed that barriers to diagnosis present significant challenges, particularly in rural and remote areas. Delayed referrals are a major issue, cited by 75% of respondents, often due to limited access to specialized diagnostic facilities. Geographical accessibility exacerbates the problem, as patients in remote regions struggle to reach centers offering advanced tests like TRAbs and nuclear scans. Additionally, over-testing in the private sector contrasts with underdiagnosis in rural areas, highlighting disparities in healthcare access. A lack of awareness about hyperthyroidism symptoms among both patients and primary care physicians further contributes to delayed diagnosis, underscoring the need for improved education and resource allocation.

One study aimed to assess knowledge about hypothyroidism and hyperthyroidism among Saudi adults through a cross-sectional survey conducted from December 2022 to January 2023, involving 996 participants (66.2% women) across five regions. Results showed that 70.1% knew the thyroid gland's function, 66.4% recognized women's higher susceptibility, and 49.5% understood the link between thyroid dysfunction and heart disease. Knowledge was higher among older, educated women, but overall awareness was inadequate, with significant gaps in certain populations. The study highlights the need for larger future studies and public health strategies to improve thyroid disease awareness and diagnosis in Saudi Arabia [1].

Another study assessed awareness of thyroid diseases and their risk factors among residents of Jeddah, Saudi Arabia, through a cross-sectional survey conducted from January to December 2023. A self-administered online questionnaire, translated into Arabic, was completed by 393 participants (72.5% female, 27.5% male), most of whom held a bachelor's degree or higher (78.1%). Results revealed that only 20% of participants had good knowledge about thyroid diseases, with hypothyroidism being the most prevalent diagnosed condition (14%). Awareness was particularly low regarding risks during pregnancy and postpartum (35%), medications like amiodarone (26%), soy consumption (22%), and gastrointestinal symptoms of thyroid diseases (36%). Attitudes toward thyroid health were largely negative (85.5%), though a history of thyroid disease was associated with more positive attitudes ($p = 0.002$). Educational level and employment status significantly influenced knowledge ($p = 0.036$ and 0.005, respectively), and a positive correlation was found between knowledge and attitudes ($r = 0.321$, $p < 0.001$). The study concluded that awareness was low, especially among the unemployed and less educated, highlighting the need for public health campaigns to address gaps in knowledge [2].

5. Subclinical Hyperthyroidism

Subclinical hyperthyroidism may resolve on its own but progresses to overt hyperthyroidism in about 8% of patients at 1 year and 26% by 5 years, particularly in those with undetectable baseline TSH or toxic multinodular goiter [21] [22]. Subclinical hyperthyroidism is associated with increased risks of atrial fibrillation, heart failure, cardiovascular mortality, and fractures, especially when TSH levels are <0.1 mIU/L [23] [24].

Excess thyroid hormone accelerates bone resorption, leading to a 3 - 4-fold increase in hip and spinal fracture risks in postmenopausal women and a 36% higher hip fracture risk overall. A trial comparing RAI and ATD in older adults with subclinical hyperthyroidism found no significant differences in bone density or echocardiography results, with most RAI-treated patients becoming hypothyroid and most ATD-treated patients remaining euthyroid [25].

The US Preventive Services Task Force does not recommend routine testing or treatment for subclinical hyperthyroidism, but other US and European guidelines suggest treatment for patients over 65 (or younger patients with symptoms, osteoporosis, or heart disease) when TSH is consistently < 0.1 mIU/L. Treatment may also be considered for TSH levels between 0.1 - 0.4 mIU/L in these groups, but it is generally avoided in asymptomatic patients under 65 without osteoporosis or heart disease. Additionally, clinicians should rule out exogenous subclinical hyperthyroidism caused by excessive thyroid hormone replacement or factitious thyrotoxicosis before initiating treatment [16] [26].

6. Treatment Challenges

Untreated overt thyrotoxicosis, particularly in older individuals, can lead to serious complications such as osteoporosis, atrial fibrillation, and, rarely, high-output heart failure because of the effects of excess thyroid hormone on thyroid hormone receptors in bone and heart tissues. Atrial fibrillation occurs in 10% - 25% of patients with thyrotoxicosis, with higher risks in men and those aged over 65 years [27].

Treatment should be patient-centered and individualized, considering factors such as age, comorbidities, severity of hyperthyroidism, likelihood of remission, pregnancy plans, surgical expertise, and patient preferences [28].

The underlying etiology of hyperthyroidism should guide treatment decisions; for Graves' disease, the focus is on controlling hyperthyroidism with the expectation of eventual remission, whereas toxic nodular disease requires indefinite treatment if ATDs are used, as it does not remit. Symptomatic patients with thyrotoxicosis may benefit from beta blockers to reduce heart rate and alleviate hyperadrenergic symptoms, though these are relatively contraindicated in patients with bronchospastic disease [29]. Beta blockade alone is often sufficient for thyroiditis-induced thyrotoxicosis, as it is self-limiting and does not require ATDs unless thyroid hormone synthesis is increased [16].

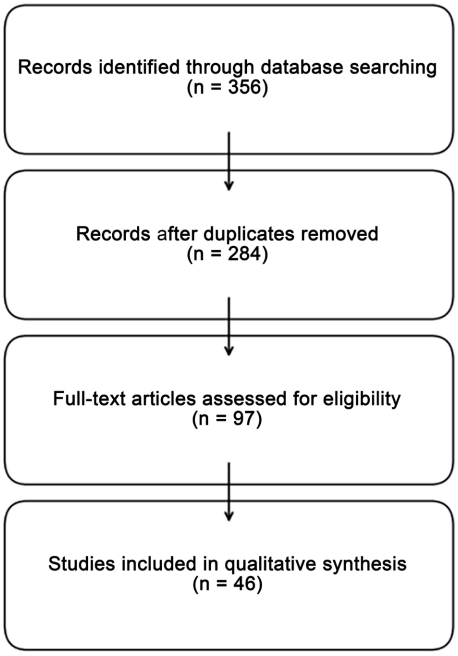

Figure 2. PRISMA flow diagram.

Most patients with overt hyperthyroidism caused by autonomous thyroid nodules or Graves' disease require treatment with ATDs, radioactive iodine ablation, or surgery [3]. In the US, practice patterns have shifted toward prioritizing ATDs over radioactive iodine as the initial treatment, aligning more closely with practices in other regions [30].

According to the surveyed doctors in the current study, antithyroid drugs (ATDs) are universally used by clinicians (100%) for managing uncomplicated hyperthyroidism, with 75% preferring carbimazole and 25% opting for methimazole, primarily due to availability and clinical experience. ATDs are consistently prescribed before radioiodine therapy in all cases.

Thionamides, including methimazole (MMI), carbimazole (CBZ), and propylthiouracil (PTU), reduce thyroid hormone synthesis and secretion, restoring euthyroidism in hyperthyroid patients. MMI or CBZ is the first-line agent, except in the first trimester of pregnancy [16]. MMI dosing is based on free T4 (FT4) levels: 5 - 10 mg/day for FT4 1.0 - 1.5 times the upper limit of normal (ULN), 10 - 20 mg/day for FT4 1.5 - 2.0 times ULN, and 30 - 40 mg/day for FT4 2 - 3 times ULN [16]. CBZ is converted to MMI in the body, but at a lower concentration (10 mg CBZ is equivalent to 6 - 7 mg MMI) [31]. Thyroid function tests (TFTs) should be monitored every 4 - 8 weeks initially, with MMI often tapered to 5 - 10 mg/day as hyperthyroidism improves. High-dose ATDs with levothyroxine ("block and replace") are not routinely recommended due to increased toxicity risks without clear benefits [32].

For autonomous thyroid nodules, MMI doses are typically ≤ 10 mg/day, with TFTs monitored every 3 months initially [16]. In Graves' disease, ATDs can be discontinued after 12 - 18 months if TSH normalizes and TRAbs are negative,

with remission rates of 30% - 50% after initial treatment [16] [33] [34].

Mahzari *et al.* (2024), conducted a retrospective chart review of 189 Graves' disease patients treated with anti-thyroid drugs (ATD) between 2015-2022 at King Abdulaziz Medical City, Riyadh. The study found that 54.5% achieved remission, but about one-third later relapsed. Lower free T4 and TRAb levels at diagnosis were linked to remission, while longer ATD use and higher thyroid uptake were predictors of relapse. The authors concluded that although ATD achieved remission in about half of patients, relapse remained common, highlighting the need for further research to clarify predictors of long-term treatment success [35].

Remission likelihood increases with longer ATD use (up to 80% - 85% after >5 years), but is lower in younger patients, those with higher baseline thyroid hormone levels, elevated TRAb titers, or larger goiters [36]-[39]. Hyperthyroidism recurrence is most likely within 6 months of ATD discontinuation, especially if TRAb remains elevated. Definitive therapy (radioactive iodine or thyroidectomy) is recommended for non-remission or recurrence after 12 - 18 months, though long-term MMI use (up to 24 years) is safe and effective [16] [36] [37]. TRAb titers and TFTs should be monitored every 1 - 2 years and 4 - 6 months, respectively, during long-term ATD therapy [16].

Adverse effects occur in ~13% of patients, with pruritus/rash being most common (6% on MMI and CBZ, 3% on PTU), often managed with antihistamines [16] [40]. Rare side effects include agranulocytosis (0.2% - 0.5%), typically within 90 days of initiation, and hepatitis (2.7% on PTU, 0.4% on MMI and CBZ), with liver injury risk highest in the first 90 days [40]-[42]. PTU carries a risk of fulminant hepatic failure, while both ATDs can cause antineutrophil cytoplasmic antibody-associated vasculitis (3% risk, higher with PTU) [43]. Pancreatitis, a newly recognized MMI/CBZ risk in Europe, has an absolute risk of <0.4% over 18 months [44] [45]. Baseline CBC and LFTs are recommended before ATD initiation, though the benefit of ongoing monitoring is unclear [16]. Uncontrolled hyperthyroidism often causes abnormal LFTs (55% at baseline), which typically normalize after ATD treatment [46]. Patients should be counseled on potential adverse effects before starting ATDs [16] [37].

Radioactive iodine (RAI) treatment effectively cures hyperthyroidism in over 90% of patients with Graves' disease or autonomous thyroid nodules [30] [47]. Persistent hyperthyroidism after RAI in Graves' disease is associated with male sex, prior antithyroid ATD therapy, delayed treatment (>6 months post-diagnosis), elevated FT4 levels, larger thyroid volume, and higher RAI uptake [48]. Beta blockers and pre-treatment ATDs are recommended for older patients or those at high cardiovascular risk to manage transient hyperthyroidism post-RAI. MMI/CBZ should be stopped 2 - 7 days before RAI and restarted 3 - 7 days post-treatment [16] [49]. The goal of RAI in Graves' disease is to induce hypothyroidism, while in toxic nodular goiter, it is to alleviate hyperthyroidism. Hypothyroidism risk after RAI for autonomous nodules depends on the administered dose, reaching up to 60% [50] [51]. Post-RAI, thyroid function tests should be monitored every

4 - 6 weeks for 6 months or until stable hypothyroidism is achieved. Persistent hyperthyroidism after 6 months may require repeat RAI [16].

RAI can exacerbate Graves' eye disease, especially in smokers or those with high TRAb levels. Pretreatment with prednisone (0.3 - 0.5 mg/kg/day, tapered over 3 months) is recommended for these patients [52]. The long-term cancer risk associated with RAI remains unclear, with a meta-analysis of 479,452 patients showing no significant overall cancer risk increase. However, a dose-response association was noted between RAI therapy and mortality from breast and other solid tumors [53].

Thyroidectomy is recommended for hyperthyroidism patients with large goiters causing compressive symptoms, suspicious or malignant thyroid nodules, or moderate to severe Graves ophthalmopathy. It is the first-line treatment if thyroid malignancy is suspected or confirmed. For Graves' disease, total thyroidectomy is preferred over subtotal thyroidectomy due to a lower risk of recurrent hyperthyroidism, while thyroid lobectomy may be chosen for toxic adenoma when rapid resolution, cosmesis, or compressive symptoms are concerns. Although total thyroidectomy effectively cures hyperthyroidism, it necessitates lifelong thyroid hormone replacement and carries risks such as recurrent laryngeal nerve damage, hematoma, and hypoparathyroidism, with higher complication rates among less experienced surgeons. Preoperative ATDs reduce the risk of thyroid storm, and high-dose iodine can decrease thyroid vascularity and operative blood loss in Graves' disease patients, though it may not affect postoperative complication risks. Additionally, preoperative calcium and/or vitamin D supplementation may help reduce the risk of postoperative hypocalcemia [16] [17].

Radiofrequency ablation (RFA) is a minimally invasive alternative to surgery or radioactive iodine for treating toxic thyroid nodules, particularly in selected centers. This technique uses heat energy to induce tissue necrosis, reducing nodule volume by 52% - 86% and normalizing thyroid function in 61.7% of cases (95% CI: 48.7% - 74.7%). Guidelines recommend RFA primarily for younger patients with small nodules, though it may also be considered for those with larger toxic multinodular goiters who are unsuitable for surgery or radioactive iodine. Additionally, novel therapies for Graves' disease, such as small molecules, biologics, and immunomodulatory peptides targeting the TSH receptor, are currently under investigation, offering potential future advancements in treatment [16] [17].

However, according to the current expert panel, treatment challenges persist, including limited access to medications, especially in rural areas, non-adherence to treatment and follow-up, and the absence of clear national guidelines for managing hyperthyroidism in special populations such as pregnant women and elderly patients. These barriers highlight the need for improved resource allocation, patient education, and standardized guidelines to enhance care for hyperthyroidism patients.

According to experts in our current study, current referral practices for hyperthyroidism in Saudi Arabia reveal significant inefficiencies, particularly in rural

areas where delays in accessing specialist care are common due to geographical barriers and limited healthcare infrastructure. In contrast, urban areas experience over-referral and over-testing, with primary care physicians (PCPs) often referring mild or borderline cases to specialists unnecessarily. Additionally, other health care specialists frequently request thyroid tests without clear indications, contributing to overdiagnosis and straining healthcare resources. These disparities highlight the need for a more balanced and efficient referral system.

To address these challenges, several solutions have been proposed. Standardized referral algorithms could guide PCPs in determining when specialist consultations are truly necessary, reducing both delays in rural areas and over-referral in urban centers. Virtual consultations could further streamline access to specialist advice, minimizing unnecessary in-person visits and improving efficiency. Enhancing PCP education on recognizing and managing hyperthyroidism is also critical, as it would empower primary care providers to handle milder cases independently and refer only when appropriate. These measures could help bridge regional disparities and optimize the management of hyperthyroidism across Saudi Arabia.

Managing hyperthyroidism in Saudi Arabia presents several challenges, particularly in ensuring timely diagnosis and access to specialized care. One significant issue is the delayed diagnosis due to limited awareness among patients and PCPs about hyperthyroidism symptoms. This delay is exacerbated in rural areas, where access to diagnostic facilities and specialized tests, such as TRAb testing and nuclear scans, is limited. Over-reliance on private healthcare in urban areas can lead to over-testing, while rural regions face underdiagnosis due to resource constraints. These disparities highlight the need for improved public health campaigns and better distribution of diagnostic resources across the country [54].

Another challenge is the limited availability of ATDs and other treatment options, particularly in remote areas. While ATDs like CBZ, MMI, and PTU are commonly used, their accessibility is inconsistent, leading to non-adherence and interrupted treatment. Additionally, there is a lack of clear national guidelines for managing hyperthyroidism in special populations, such as pregnant women and the elderly. This gap in standardized care can result in suboptimal treatment outcomes and increased risks of complications, such as congenital anomalies in pregnant women or cardiovascular issues in older patients [54].

Finally, patient education and follow-up remain critical challenges. Many patients lack awareness of the importance of medication adherence and the potential side effects of hyperthyroidism treatments, such as agranulocytosis or liver injury. Regular monitoring of thyroid function tests and patient adherence to treatment plans are often inadequate, particularly in underserved areas. Addressing these challenges requires a multifaceted approach, including public health initiatives to raise awareness, improved access to medications and diagnostic tools, and the development of clear, standardized guidelines for managing hyperthyroidism across diverse patient populations [54].

7. Hyperthyroidism in Pregnant Women

The current study showed that treatment preferences for hyperthyroidism during pregnancy vary. About 50% of clinicians use CBZ, 25% use MMI, and 25% prefer PTU, with PTU being favored in early pregnancy due to the higher risk of congenital anomalies associated with CBZ and MMI.

Gestational transient thyrotoxicosis (GTT), caused by elevated hCG levels stimulating the thyroid gland, affects 2% - 11% of pregnancies and is often linked to hyperemesis gravidarum [55]. Unlike other forms of hyperthyroidism, GTT does not require ATD treatment and is not associated with adverse obstetric outcomes [56]. It can be managed with serial thyroid function tests and typically resolves spontaneously as hCG levels decline [57] [58].

However, all other forms of overt hyperthyroidism in pregnancy require treatment to mitigate risks such as preeclampsia, low birth weight, miscarriage, and preterm delivery [59]. ATDs, including PTU, CBZ, and MMI, are teratogenic, but PTU is associated with milder congenital anomalies (e.g., facial or neck cysts, urinary tract abnormalities) compared to MMI/CBZ, which are linked to more severe defects like aplasia cutis and esophageal atresia [60]. PTU is therefore preferred in the first trimester, with the lowest effective dose used to maintain maternal FT4 levels at or just above the upper reference limit, as ATDs can significantly affect fetal thyroid function [57] [58]. Moreover, ATDs are secreted in breast milk at low levels, but doses up to 20 mg/day of MMI (around 30 mg of CBZ) and 450 mg/day of PTU are considered safe during lactation and do not require thyroid function monitoring in breastfed infants [58].

Radioactive iodine (RAI) treatment is contraindicated during pregnancy and lactation and should be deferred until at least 3 months after breastfeeding ends to avoid radiation exposure to breast tissue [57] [61]. If necessary, thyroidectomy is safest during the second trimester of pregnancy [62]. These notions emphasize the importance of balancing maternal and fetal safety while managing hyperthyroidism in pregnancy and lactation.

8. Hyperthyroidism in Elderly Patients

Studies have shown that thyroid function, including levels of TSH, FT4, and FT3, changes with aging, though interpretations of these changes remain controversial [63]-[65]. Hyperthyroidism in the elderly presents diagnostic challenges due to atypical symptoms, often leading to delayed diagnosis and worse outcomes [66] [67]. Unlike younger patients, elderly individuals may not exhibit classic hyperthyroidism symptoms like tachycardia or heat intolerance but instead present with atrial fibrillation, heart failure, weight loss, osteoporosis, or depression [68]. Clinicians must differentiate true hyperthyroidism from non-thyroidal illness, which can also suppress TSH levels in acutely ill elderly patients [69].

The American Thyroid Association (ATA) recommends a two-step approach to treating hyperthyroidism: rapid symptom control and reducing thyroid hormone synthesis [16]. Beta-blockers are first-line for symptom management, par-

ticularly in elderly patients with a resting heart rate over 90 bpm or cardiovascular disease, as they improve heart rate, blood pressure, and symptoms such as tremors and irritability [70].

Glucocorticoids may also help by inhibiting T4-to-T3 conversion. Treatment options for Graves' disease include ATDs, radioactive iodine ablation, and thyroidectomy, with methimazole being the preferred ATD for elderly patients due to its efficacy [71]. However, older adults are at higher risk of side effects such as agranulocytosis (0.5% risk), rash, and liver injury, necessitating baseline blood tests and regular monitoring of FT4 and T3 levels. Also, serum TSH is not reliable for early monitoring, as it may remain suppressed for months after treatment initiation. Personalized treatment is essential to balance efficacy and safety in this population [16].

Recommendations

Most important recommendations are mentioned in Table 2.

Table 2. Actionable recommendation.

Domain	Recommendation (Consensus ≥ 75%)
Diagnosis	TSH as first-line; TRAb where available; Ultrasound in nodular disease
First-line therapy	Methimazole (preferrable); Carbimazol; Propylthiouracil in 1st trimester of pregnancy or methimazole intolerance
Radioiodine therapy	Consider for recurrent Graves' disease; availability to be expanded in tertiary centers
Surgery	Reserved for large goiters, suspicion of malignancy, or failed medical/RIA therapy
Follow-up	Every 6 - 8 weeks until stable; then 6 - 12 months depending on disease status
Special populations	Pregnancy: PTU in 1st trimester, switch to methimazole thereafter; Elderly: individualized therapy
Supportive care	Patient education materials; referral networks; emphasize adherence and monitoring
System-level needs	Establish national registry; implement CME/educational programs; update guidelines biennially

The entire developed recommendations are shown in Table 3.

Table 3. All recommendations.

	Recommendation	Evidence level
1	The etiology of thyrotoxicosis should be determined. If the diagnosis is unclear based on clinical presentation and initial biochemical evaluation, diagnostic testing such as TRAb measurement, radioactive iodine uptake (RAIU)/scan or 99mTc pertechnetate scan, or thyroidal blood flow on ultrasonography should be performed.	Evidence: Strong recommendation, moderate-quality evidence.
2	Beta-adrenergic blockade is recommended for all symptomatic thyrotoxic patients, especially elderly patients and those with resting heart rates > 90 beats per minute or coexistent cardiovascular disease.	Evidence: Strong recommendation, moderate-quality evidence.

Continued

3	Patients with overt Graves' hyperthyroidism should be treated with radioactive iodine (RAI) therapy, antithyroid drugs (ATDs), or thyroidectomy.	Evidence: Strong recommendation, moderate-quality evidence.
4	RAI treatment for Graves' disease (GD) can transiently worsen hyperthyroidism, so beta-blockers should be considered for asymptomatic patients at increased risk of complications, such as the elderly or those with comorbidities.	Evidence: Weak recommendation, low-quality evidence.
5	Pretreatment with antithyroid drugs (ATDs) before RAI therapy is recommended for GD patients at risk of complications from worsening hyperthyroidism. ATDs should be stopped 2 - 3 days before RAI.	Evidence: Weak recommendation, moderate-quality evidence.
6	ATDs should be resumed 3 - 7 days after RAI administration in patients at increased risk of complications from worsening hyperthyroidism.	Evidence: Weak recommendation, low-quality evidence.
7	Optimize medical therapy for comorbid conditions before RAI therapy.	Evidence: Strong recommendation, low-quality evidence.
8	A single dose of RAI (10 - 15 mCi or 370 - 555 MBq) should be administered to render GD patients hypothyroid.	Evidence: Strong recommendation, moderate-quality evidence.
9	A pregnancy test must be performed within 48 hours before RAI therapy for women of childbearing potential.	Evidence: Strong recommendation, low-quality evidence.
10	Provide written radiation safety precautions after RAI therapy. If the precautions cannot be followed, alternative treatments should be considered.	Evidence: Strong recommendation, low-quality evidence.
11	Follow-up within 1 - 2 months after RAI therapy for GD should include free T4, free T3, and TSH measurements, with monitoring every 4 - 6 weeks for 6 months or until the patient becomes hypothyroid.	Evidence: Strong recommendation, low-quality evidence.
12	If hyperthyroidism persists 6 months after RAI therapy, retreatment with RAI is suggested. Additional RAI may be considered 3 months post-therapy in selected patients.	Evidence: Weak recommendation, low-quality evidence.
13	MMI or CBZ is the preferred ATD for GD, except in the first trimester of pregnancy, thyroid storm, or in patients with minor reactions to MMI/CBZ who refuse RAI or surgery.	Evidence: Strong recommendation, moderate-quality evidence.
14	Patients should be informed of ATD side effects and instructed to stop medication and contact their physician if symptoms of agranulocytosis or hepatic injury occur.	Evidence: Strong recommendation, low-quality evidence.
15	Baseline complete blood count (CBC) and liver function tests (LFTs) should be obtained before starting ATD therapy.	Evidence: Weak recommendation, low-quality evidence.
16	A differential white blood cell (WBC) count should be obtained during febrile illness or pharyngitis in patients taking ATDs.	Evidence: Strong recommendation, low-quality evidence.
17	Routine monitoring of WBC counts in patients taking ATDs is not recommended.	Evidence: No recommendation; insufficient evidence.
18	Liver function tests should be assessed in patients taking ATDs who develop symptoms of hepatic injury.	Evidence: Strong recommendation, low-quality evidence.
19	Routine monitoring of liver function tests in patients taking ATDs is not recommended.	Evidence: No recommendation; insufficient evidence.

Continued

20	Minor cutaneous reactions to ATDs may be managed with antihistamines. Persistent side effects should prompt cessation of the ATD and consideration of RAI or surgery.	Evidence: Strong recommendation, low-quality evidence.
21	TRAb levels should be measured before stopping ATD therapy to predict the likelihood of remission.	Evidence: Strong recommendation, moderate-quality evidence.
22	Thionamide therapy for GD should be continued for 12 - 18 months and discontinued if TSH and TRAb levels are normal.	Evidence: Strong recommendation, high-quality evidence.
23	If hyperthyroidism recurs after therapy with ATDs, RAI or thyroidectomy should be considered. Long-term low-dose ATDs may be used in patients not in remission who prefer this approach.	Evidence: Weak recommendation, low-quality evidence.
24	Patients undergoing thyroidectomy for GD should be rendered euthyroid with ATDs and beta-blockers preoperatively, with potassium iodide (KI) given immediately before surgery.	Evidence: Strong recommendation, low-quality evidence.
25	Preoperative calcium and vitamin D assessment and supplementation are recommended, with calcitriol considered for patients at risk of hypoparathyroidism.	Evidence: Strong recommendation, low-quality evidence.
26	In urgent cases where euthyroidism cannot be achieved preoperatively, patients should be treated with beta-blockers, KI, glucocorticoids, and potentially cholestyramine.	Evidence: Strong recommendation, low-quality evidence.
27	Near-total or total thyroidectomy is the preferred surgical procedure for GD.	Evidence: Strong recommendation, moderate-quality evidence.
28	Thyroidectomy for GD should be performed by a high-volume thyroid surgeon.	Evidence: Strong recommendation, moderate-quality evidence.
29	Post-thyroidectomy calcium management may include serum calcium and intact parathyroid hormone (iPTH) measurements, with oral calcium and calcitriol supplementation as needed.	Evidence: Weak recommendation, low-quality evidence.
30	ATDs should be stopped at the time of thyroidectomy, and beta-blockers should be weaned postoperatively.	Evidence: Strong recommendation, low-quality evidence.
31	L-thyroxine should be started post-thyroidectomy at a dose of 1.6 μg/kg, with TSH measured 6 - 8 weeks postoperatively.	Evidence: Strong recommendation, low-quality evidence.
32	Effective communication among the multidisciplinary team is essential during pre- and postoperative care transitions.	Evidence: Strong recommendation, low-quality evidence.
33	Thyroid nodules in GD patients should be evaluated and managed according to guidelines for euthyroid individuals.	Evidence: Strong recommendation, moderate-quality evidence.
34	Thyroid storm should be diagnosed clinically in severely thyrotoxic patients with systemic decompensation, using tools such as the Burch-Wartofsky Point Scale (BWPS) or Japanese Thyroid Association (JTA) criteria.	Evidence: Strong recommendation, moderate-quality evidence.
35	A multimodal approach, including beta-blockers, ATDs, inorganic iodide, corticosteroids, and supportive care, should be used for thyroid storm.	Evidence: Strong recommendation, low-quality evidence.
36	TMNG or TA should be treated with RAI or thyroidectomy, with long-term low-dose ATDs considered in selected cases.	Evidence: Weak recommendation, moderate-quality evidence.
37	Beta-blockers should be considered for asymptomatic TMNG or TA patients at risk of complications from worsening hyperthyroidism.	Evidence: Weak recommendation, low-quality evidence.

Continued

38	Pretreatment with ATDs before RAI therapy is recommended for TMNG or TA patients at risk of complications.	Evidence: Weak recommendation, low-quality evidence.
39	ATDs should be resumed 3 - 7 days after RAI therapy in TMNG or TA patients at risk of complications.	Evidence: Weak recommendation, low-quality evidence.
40	Nonfunctioning or suspicious thyroid nodules should be managed according to guidelines for euthyroid individuals.	Evidence: Strong recommendation, moderate-quality evidence.
41	A single dose of RAI should be administered to alleviate hyperthyroidism in TMNG patients.	Evidence: Strong recommendation, moderate-quality evidence.
42	A single dose of RAI should be administered to alleviate hyperthyroidism in TA patients.	Evidence: Strong recommendation, moderate-quality evidence.
43	Follow-up within 1 - 2 months after RAI therapy for TMNG or TA should include free T4, free T3, and TSH measurements, with monitoring every 4 - 6 weeks for 6 months or until hypothyroidism is achieved.	Evidence: Strong recommendation, low-quality evidence.
44	If hyperthyroidism persists for 6 months after RAI therapy for TMNG or TA, retreatment with RAI is suggested.	Evidence: Weak recommendation, low-quality evidence.
45	TMNG or TA patients undergoing surgery should be rendered euthyroid with ATDs preoperatively, without preoperative iodine.	Evidence: Strong recommendation, low-quality evidence.
46	Near-total or total thyroidectomy is recommended for TMNG.	Evidence: Strong recommendation, moderate-quality evidence.
47	TMNG surgery should be performed by a high-volume thyroid surgeon.	Evidence: Strong recommendation, moderate-quality evidence.
48	Thyroid ultrasound should be performed before TA surgery, with ipsilateral lobectomy or isthmusectomy recommended for isolated TAs.	Evidence: Strong recommendation, moderate-quality evidence.
49	TA surgery should be performed by a high-volume surgeon.	Evidence: Weak recommendation, moderate-quality evidence.
50	Post-thyroidectomy calcium management for TMNG should include serum calcium and iPTH measurements, with oral calcium and calcitriol supplementation as needed.	Evidence: Weak recommendation, low-quality evidence.
51	ATDs should be stopped at the time of TMNG or TA surgery, and beta-blockers should be weaned postoperatively.	Evidence: Strong recommendation, low-quality evidence.
52	L-thyroxine should be started post-thyroidectomy for TMNG at a dose of 1.6 μg/kg, with TSH monitored every 6 - 8 weeks until stable.	Evidence: Strong recommendation, low-quality evidence.
53	TSH and free T4 should be measured 4 - 6 weeks after lobectomy for TA, with thyroid hormone supplementation started if TSH rises above the reference range.	Evidence: Strong recommendation, low-quality evidence.
54	RAI therapy should be used for persistent or recurrent hyperthyroidism after inadequate TMNG or TA surgery.	Evidence: Strong recommendation, low-quality evidence.
55	Long-term therapy with ATDs may be considered for TMNG or TA in elderly or ill patients with limited life expectancy or those who are not candidates for surgery or RAI.	Evidence: Weak recommendation, low-quality evidence.
56	Alternative therapies such as ethanol or radiofrequency ablation may be considered for TA or TMNG in select patients.	Evidence: No recommendation; insufficient evidence.

Continued

57	Children with GD should be treated with MMI or CBZ, RAI, or thyroidectomy. RAI should be avoided in children < 5 years and used cautiously in children 5 - 10 years.	Evidence: Strong recommendation, moderate-quality evidence.
58	MMI or CBZ is the preferred ATD for children with GD.	Evidence: Strong recommendation, moderate-quality evidence.
59	Pediatric patients and caregivers should be informed of ATD side effects and instructed to stop medication if symptoms of agranulocytosis or hepatic injury occur.	Evidence: Strong recommendation, low-quality evidence.
60	Baseline CBC and LFTs should be obtained before starting ATD therapy in children.	Evidence: Weak recommendation, low-quality evidence.
61	Beta-blockers are recommended for children with hyperthyroidism and heart rates >100 beats per minute.	Evidence: Strong recommendation, low-quality evidence.
62	ATDs should be stopped immediately, and WBC counts measured in children with fever, arthralgia, pharyngitis, or malaise.	Evidence: Strong recommendation, low-quality evidence.
63	PTU should not be used in children. If used, it should be stopped immediately if symptoms of hepatic injury occur.	Evidence: Strong recommendation, low-quality evidence.
64	Minor cutaneous reactions to ATDs in children should be managed with antihistamines or by switching to RAI or surgery.	Evidence: Strong recommendation, low-quality evidence.
65	Therapy with ATDs for GD in children may be tapered after 1 -2 years to assess remission or continued until definitive therapy is considered.	Evidence: Strong recommendation, moderate-quality evidence.
66	Children not in remission after 1 - 2 years of therapy with ATDs should be considered for RAI or thyroidectomy. Long-term ATD therapy may be used in selected cases.	Evidence: Strong recommendation, low-quality evidence.
67	Children with GD and high T4 levels should be pretreated with ATDs and beta-blockers before RAI therapy.	Evidence: Weak recommendation, low-quality evidence.
68	A single dose of RAI should be administered to render GD children hypothyroid.	Evidence: Strong recommendation, moderate-quality evidence.
69	Children undergoing thyroidectomy for GD should be rendered euthyroid with ATDs and given KI preoperatively.	Evidence: Strong recommendation, low-quality evidence.
70	Total or near-total thyroidectomy is recommended for GD in children.	Evidence: Strong recommendation, moderate-quality evidence.
71	Thyroidectomy in children should be performed by a high-volume thyroid surgeon.	Evidence: Strong recommendation, moderate-quality evidence.
72	Treatment of subclinical hyperthyroidism (SH) is recommended for patients ≥ 65 years, those with cardiac risk factors, osteoporosis, or hyperthyroid symptoms, and postmenopausal women not on estrogen or bisphosphonates.	Evidence: Strong recommendation, moderate-quality evidence.
73	Treatment of SH should be considered for asymptomatic patients < 65 years without risk factors.	Evidence: Weak recommendation, moderate-quality evidence.
74	Treatment of SH should be considered for patients ≥ 65 years or those with cardiac disease, osteoporosis, or hyperthyroid symptoms when TSH is persistently below the lower limit of normal but ≥0.1 mU/L.	Evidence: Weak recommendation, moderate-quality evidence.

Continued

75	Asymptomatic patients < 65 years without cardiac disease or osteoporosis can be observed without treatment when TSH is persistently below the lower limit of normal but ≥0.1 mU/L.	Evidence: Weak recommendation, low-quality evidence.
76	Treatment of SH should follow the same principles as overt hyperthyroidism, based on the etiology.	Evidence: Strong recommendation, low-quality evidence.
77	Hyperthyroidism in pregnancy should be diagnosed using trimester-specific TSH, free T4, and free T3 reference ranges.	Evidence: Strong recommendation, low-quality evidence.
78	Transient hCG-mediated TSH suppression in early pregnancy should not be treated with ATDs.	Evidence: Strong recommendation, low-quality evidence.
79	PTU should be used for ATD therapy in the first trimester of pregnancy, and MMI or CBZ should be used after the first trimester.	Evidence: Strong recommendation, low-quality evidence.
80	Women with hyperthyroidism should postpone pregnancy until they are euthyroid.	Evidence: Strong recommendation, low-quality evidence.
81	Women requiring high ATD doses to achieve euthyroidism should consider definitive therapy before pregnancy.	Evidence: Weak recommendation, low-quality evidence.
82	Women with GD well-controlled on ATDs who desire pregnancy have several options, including switching to PTU or withdrawing ATD therapy.	Evidence: Weak recommendation, low-quality evidence.
83	Women on ATDs who may become pregnant should perform a pregnancy test after a missed or light menstrual period.	Evidence: Weak recommendation, low-quality evidence.
84	Women who test positive for pregnancy should contact their physician within 24 hours to discuss treatment options.	Evidence: Weak recommendation, low-quality evidence.
85	The decision to withdraw ATDs in early pregnancy should be based on the risk of relapse, assessed using the patient's history and recent thyroid function tests.	Evidence: Weak recommendation, low-quality evidence.
86	Women at high risk of hyperthyroidism relapse in early pregnancy should switch from MMI or CBZ to PTU immediately after pregnancy is diagnosed.	Evidence: Weak recommendation, low-quality evidence.
87	Women taking PTU in the first trimester may switch to MMI or CBZ in the second trimester, or continue PTU.	Evidence: No recommendation; insufficient evidence.
88	GD during pregnancy should be treated with the lowest effective ATD dose to keep maternal thyroid hormone levels slightly above the pregnancy reference range.	Evidence: Strong recommendation, low-quality evidence.
89	Pregnancy is a relative contraindication to thyroidectomy, which should only be used if medical management fails or ATDs cannot be used.	Evidence: Strong recommendation, low-quality evidence.
90	Thyroidectomy during pregnancy should be performed in the second trimester if possible.	Evidence: Strong recommendation, low-quality evidence.
91	TRAb levels should be measured when the etiology of hyperthyroidism in pregnancy is uncertain.	Strong recommendation, low-quality evidence.
92	Patients who were treated with RAI or thyroidectomy for GD prior to pregnancy should have TRAb levels measured using a sensitive assay initially during the first trimester thyroid function testing and, if levels are elevated, again at 18 - 22 weeks of gestation.	Strong recommendation, low-quality evidence.
93	Patients receiving ATD for GD when becoming pregnant or found to have GD during pregnancy should have TRAb levels measured at the initial pregnancy visit or at diagnosis using a sensitive assay and, if they are elevated, again at 18 - 22 weeks of gestation.	Strong recommendation, low-quality evidence.

Continued

94	Patients with elevated TRAb levels at 18 - 22 weeks of gestation should have TRAb remeasured in late pregnancy (weeks 30 - 34) to guide decisions regarding neonatal monitoring. An exception to this recommendation is a woman with an intact thyroid who is no longer in need of ATD therapy.	Strong recommendation, low-quality evidence.
95	In women developing thyrotoxicosis after delivery, selective diagnostic studies should be performed to distinguish postpartum destructive thyroiditis from postpartum GD.	Strong recommendation, low-quality evidence.
96	In women with symptomatic thyrotoxicosis from postpartum destructive thyroiditis, the judicious use of β-adrenergic blocking agents is recommended.	Strong recommendation, low-quality evidence.
97	In pregnant women diagnosed with hyperthyroidism due to multinodular thyroid autonomy or a solitary TA, special care should be taken not to induce fetal hypothyroidism by ATD therapy.	Strong recommendation, low-quality evidence.
98	Euthyroidism should be expeditiously achieved and maintained in hyperthyroid patients with GO or risk factors for the development of orbitopathy.	Strong recommendation, moderate-quality evidence.
99	We recommend clinicians advise patients with GD to stop smoking and refer them to a structured smoking cessation program. As both firsthand and secondhand smoking increase GO risk, patients exposed to secondhand smoke should be identified and advised of its negative impact.	Strong recommendation, moderate-quality evidence.
100	In nonsmoking patients with GD without apparent GO, RAI therapy (without concurrent steroids), ATDs, or thyroidectomy should be considered equally acceptable therapeutic options with regard to the risk of GO.	Strong recommendation, moderate-quality evidence.
101	In smoking patients with GD without apparent GO, RAI therapy may increase the chance of developing GO. Alternative treatments for hyperthyroidism, such as ATDs or thyroidectomy, should be considered.	Weak recommendation, low-quality evidence.
102	There is insufficient evidence to recommend for or against the use of prophylactic corticosteroids in smokers who receive RAI and have no evidence of GO.	No recommendation; insufficient evidence.
103	In patients with Graves' hyperthyroidism who have mild active ophthalmopathy, RAI therapy may increase the chance of GO exacerbation. Alternative treatments for hyperthyroidism, such as ATDs or thyroidectomy, should be considered.	Strong recommendation, moderate-quality evidence.
104	In the absence of any strong contraindication to GC use, we suggest considering them for coverage of GD patients with mild active GO who are treated with RAI, even in the absence of risk factors for GO deterioration.	Weak recommendation, low-quality evidence.
105	In GD patients with mild GO who are treated with RAI, we recommend steroid coverage if there are concomitant risk factors for GO deterioration.	Strong recommendation, moderate-quality evidence.

Continued

106	In patients with active and moderate-to-severe or sight-threatening GO, we recommend against RAI therapy. Surgery or ATDs are preferred treatment options for GD in these patients.	Strong recommendation, low-quality evidence.
107	In patients with inactive GO, we suggest RAI therapy can be administered without steroid coverage. However, in cases of elevated risk for reactivation (high TRAb, CAS ≥ 1, and smokers), that approach might have to be reconsidered.	Weak recommendation, low-quality evidence.
108	Routine administration of ATDs before iodinated contrast media exposure is not recommended for all patients.	Weak recommendation, low-quality evidence.
109	Beta-adrenergic blocking agents alone or in combination with ATDs should be used to treat overt iodine-induced hyperthyroidism.	Strong recommendation, low-quality evidence.
110	We suggest monitoring thyroid function tests before and within the first 3 months following the initiation of amiodarone therapy, and at 3- to 6-month intervals thereafter.	Weak recommendation, low-quality evidence.
111	The decision to stop amiodarone in the setting of thyrotoxicosis should be determined on an individual basis in consultation with the treating cardiologist, depending on the clinical manifestations and the presence or absence of effective alternative antiarrhythmic therapy.	Strong recommendation, low-quality evidence.
112	In clinically stable patients with AIT, we suggest measuring thyroid function tests to identify disorders associated with iodine-induced hyperthyroidism (type 1 AIT), specifically including toxic nodular disease and previously occult GD.	Strong recommendation, low-quality evidence.
113	ATDs should be used to treat overt thyrotoxicosis in patients with proven underlying autonomous thyroid nodules or GD as the cause of AIT (type 1 disease), and corticosteroids should be used to treat patients with overt amiodarone-induced thyroiditis (type 2 disease).	Strong recommendation, low-quality evidence.
114	Combined ATD and corticosteroid therapy should be used to treat patients with overt AIT who are too clinically unstable to allow a trial of monotherapy, or who fail to respond to single-modality therapy, or patients in whom the etiology of thyrotoxicosis cannot be unequivocally determined.	Strong recommendation, low-quality evidence.
115	Patients with AIT who are unresponsive to aggressive medical therapy with ATDs and corticosteroids should undergo thyroidectomy.	Strong recommendation, low-quality evidence.
116	Patients with mild symptomatic subacute thyroiditis should be treated initially with β-adrenergic-blocking drugs and nonsteroidal anti-inflammatory agents (NSAIDs). Corticosteroids should be used instead of NSAIDs when patients fail to respond or present initially with moderate to severe pain and/or thyrotoxic symptoms.	Strong recommendation, low-quality evidence.
117	Patients with symptomatic thyrotoxicosis due to painless thyroiditis should be treated with β-adrenergic-blocking drugs to control symptoms.	Strong recommendation, low-quality evidence.
118	Acute thyroiditis should be treated with antibiotics and surgical drainage as determined by clinical judgment. Beta-blockers may be used to treat symptoms of thyrotoxicosis.	Strong recommendation, low-quality evidence.

Continued

119	Patients taking medications known to cause thyrotoxicosis, including interferon (IFN)-a, interleukin-2, tyrosine kinase inhibitors, and lithium, should be monitored clinically and biochemically at 6-month intervals for the development of thyroid dysfunction. Patients who develop thyrotoxicosis should be evaluated to determine the etiology and treated accordingly.	Strong recommendation, low-quality evidence.
120	The diagnosis of a TSH-secreting pituitary adenoma should be based on an inappropriately normal or elevated serum TSH level associated with elevated free T4 and free T3 concentrations, generally associated with a pituitary tumor on MRI or CT and the absence of a family history or genetic testing consistent with resistance to thyroid hormone.	Strong recommendation, low-quality evidence.
121	Patients with TSH-secreting pituitary adenomas should undergo surgery performed by an experienced pituitary surgeon.	Strong recommendation, low-quality evidence.
122	Patients with struma ovarii should initially be treated with surgical resection following preoperative normalization of thyroid hormones.	Strong recommendation, low-quality evidence.
123	Treatment of hyperthyroidism due to choriocarcinoma should include both ATDs and treatment directed against the primary tumor.	Strong recommendation, low-quality evidence.

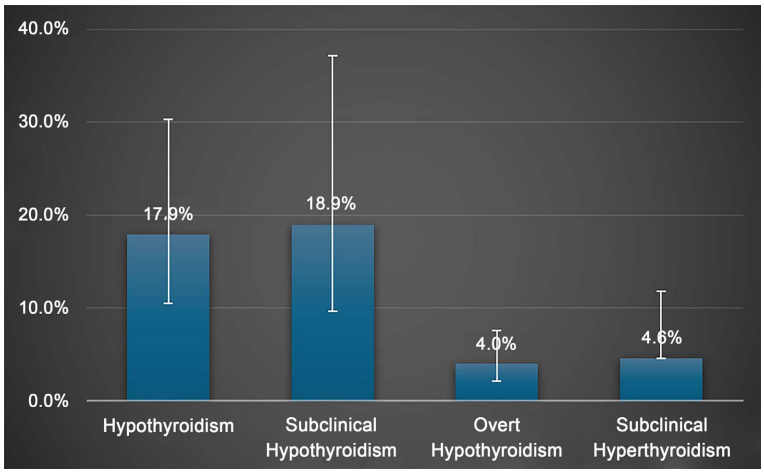

Figure 3. Prevalence of thyroid disorders in Saudi Arabia.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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