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Pediatric hyperthyroidism and its therapeutic outcomes: A comprehensive comparative review of Graves' Disease, Hashimoto's Thyroiditis, and Hashitoxicosis

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Abstract

Background: Pediatric hyperthyroidism, predominantly caused by Graves' disease (GD), is a rare endocrine disorder but has serious impacts with systemic consequences that extend beyond thyroid hormone excess. Despite the availability of antithyroid drugs (ATDs), radioactive iodine (RAI), and surgical options, controversy persists regarding optimal therapeutic strategies in children. Additionally, Hashimoto's thyroiditis (HT), while typically leading to hypothyroidism, can present with transient hyperthyroidism (Hashitoxicosis), which further complicates clinical management.

Objective: This review aimed to compare the efficacy and systemic outcomes of ATDs, RAI, and thyroidectomy in pediatric GD; to evaluate the impact of treatment on cardiac, neurological, ocular, and growth outcomes; and to define optimal strategies for managing Hashitoxicosis in children.

Methods: We conducted a comprehensive narrative review of studies published between 1998 and 2024. Data from over 60 peer-reviewed studies were analyzed, including randomized controlled trials, cohort studies, and guidelines focusing on pediatric populations with GD, HT, and Hashitoxicosis. Inclusion criteria encompassed studies reporting treatment outcomes, systemic effects, and long-term follow-up in children aged 0–18 years. Outcomes were synthesized across six domains: thyroid function, cardiovascular, neurological, ophthalmologic, linear growth, and autoimmune comorbidities.

Results: ATDs, while commonly used as first-line therapy, demonstrated remission rates of 20–30% and relapse rates up to 70%, with modest systemic recovery. RAI and thyroidectomy offered higher remission (~85–99%) and superior improvement in cardiac and neurobehavioral symptoms, linear growth, and eye signs. Thyroid surgery was most definitive but carried procedural risks. In HT-related Hashitoxicosis, the hyperthyroid phase was transient in 90–95% of cases, resolving without ATDs. Levothyroxine therapy in HT stabilized thyroid function in 70–80% of cases and improved subclinical cardiac and growth impairments. Subclinical dysfunction in euthyroid children with HT was detected via advanced imaging and improved with early therapy.

Conclusion: Effective treatment of pediatric hyperthyroidism must extend beyond biochemical control to address systemic outcomes. ATDs remain suitable for initial management, but early identification of poor responders should prompt consideration of definitive therapy. RAI and surgery are more effective in restoring multisystem stability, especially in older children. Recognition and conservative management of Hashitoxicosis, alongside timely levothyroxine initiation in HT, are crucial for optimizing outcomes. Tailored, system-informed strategies and long-term surveillance are essential in managing pediatric autoimmune thyroid disorders.

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Keywords: Graves' Disease; Hashitoxicosis; Pediatric Hyperthyroidism; Antithyroid Drugs; Radioactive Iodine; Thyroidectomy

1. Introduction

Pediatric hyperthyroidism is a rare but clinically significant endocrine disorder, most commonly caused by Graves' disease (GD), an autoimmune condition characterized by thyroid-stimulating immunoglobulins that activate the thyroid gland (1). Although less prevalent than adult-onset thyrotoxicosis, the condition in children poses unique diagnostic and therapeutic challenges due to growth, developmental, and psychosocial implications (1).

Graves' disease accounts for over 95% of hyperthyroidism cases in the pediatric population. Its incidence has increased in recent years, particularly during and after the COVID-19 pandemic, likely due to immune dysregulation triggered by viral infections (2). The disease spectrum includes cardiovascular, neurological, ophthalmologic, and growth-related consequences, all of which necessitate comprehensive management (3).

The standard first-line treatment for pediatric GD is antithyroid drugs (ATDs), particularly methimazole and carbimazole, which inhibit thyroid hormone synthesis. These medications are often well-tolerated and effective in the short term, but long-term remission remains challenging, with relapse rates after discontinuation reaching as high as 70% (4,5). Adverse effects such as agranulocytosis, hepatotoxicity, and rash may also limit prolonged use.

Radioactive iodine (RAI) therapy and surgical thyroidectomy are alternative definitive therapies used when ATDs fail or are contraindicated. RAI is typically reserved for children over 10 years and has shown high efficacy, with cure rates of 85–90%, although it carries risks such as hypothyroidism and worsening thyroid eye disease (6). Thyroidectomy, while highly effective with near 100% remission, is associated with risks like hypoparathyroidism and recurrent laryngeal nerve injury, especially when performed by less experienced surgeons (7).

Hashimoto's thyroiditis (HT), the most common cause of acquired hypothyroidism in children and adolescents, is typically characterized by elevated TSH and thyroid autoantibodies. However, a subset of pediatric patients may present with a transient hyperthyroid phase known as Hashitoxicosis, which can mimic GD but generally resolve without antithyroid therapy (8). This phase is often under-recognized, leading to unnecessary interventions.

Management of HT primarily involves L-thyroxine replacement in cases of overt or progressive subclinical hypothyroidism. Recent data show that even euthyroid children with HT may exhibit subclinical cardiac dysfunction and subtle neuropsychiatric symptoms, underscoring the need for regular surveillance and a broader treatment approach (9,10). Early L-thyroxine therapy in selected cases may help prevent long-term complications and support normal growth.

Thyroid eye disease and cognitive or behavioral issues in pediatric hyperthyroidism are often underdiagnosed. Children may present with lid lag, mild proptosis, tremors, or school difficulties before biochemical confirmation. These systemic manifestations, though less severe than in adults, can have a lasting impact on development if not addressed with a multidisciplinary care approach (11,12).

Treatment decisions in children must consider multiple variables, including age, disease severity, goiter size, antibody titers, presence of eye disease, and psychosocial context. While ATDs remain the default initial therapy, there is a growing consensus that definitive therapy may be preferable earlier in the disease course in selected patients to avoid prolonged hyperthyroidism and systemic complications (13,14).

Over the last decade, several studies have emerged comparing therapeutic modalities not only in terms of thyroid hormone normalization but also their broader systemic impacts, including cardiovascular recovery, behavioral stabilization, eye disease remission, and growth improvement. These studies support an increasingly individualized approach to treatment that balances efficacy, safety, and age-appropriateness (15,16).

Despite these advancements, important gaps remain in standardized treatment algorithms, particularly for less common scenarios like Hashitoxicosis or subclinical disease with systemic symptoms. There is a pressing need for a comprehensive review that integrates outcomes across the therapeutic spectrum of pediatric autoimmune thyroid disorders, guiding clinicians in evidence-based, holistic decision-making (17,18).

Objectives

This review was designed to address key clinical uncertainties and therapeutic controversies in the management of pediatric hyperthyroidism and autoimmune thyroid disease. The specific objectives are

- To compare the efficacy, remission, relapse, and complication profiles of antithyroid drugs, radioactive iodine, and thyroidectomy in the treatment of pediatric Graves' disease. This includes analyzing outcome data stratified by age, treatment duration, and adverse event frequency across studies published over the past two decades.
- To evaluate the systemic and extra-thyroidal effects of different therapies, including their impact on cardiac function, neurological symptoms, thyroid eye disease, and linear growth in children with hyperthyroidism. Comparative analyses were performed on outcomes observed with pharmacological, surgical, and radiological interventions.
- To define the natural history, diagnostic criteria, and optimal management strategies for children with Hashitoxicosis—transient hyperthyroidism seen in Hashimoto's thyroiditis—emphasizing the role of conservative therapy and symptom monitoring. This includes characterizing the time course of thyroid function normalization and identifying predictors for progression to hypothyroidism.

2. Materials and Methods

2.1. Study Design

This review follows a structured narrative design based on evidence synthesized from peer-reviewed clinical studies, systematic reviews, cohort studies, and expert guidelines spanning from 1998 to 2024. The methodology was designed to include comprehensive coverage of pediatric hyperthyroidism from both a disease-specific and system-wide outcome perspective.

2.2. Search Strategy

A comprehensive literature search was conducted across PubMed, Scopus, Web of Science, and Embase databases using the following Medical Subject Headings (MeSH) and keywords: "pediatric hyperthyroidism," "Graves' disease," "Hashimoto's thyroiditis," "Hashitoxicosis," "antithyroid drugs," "radioactive iodine," "thyroidectomy," "levothyroxine," "thyroid eye disease," "cardiac dysfunction," "neurocognitive symptoms," and "growth outcomes."

The search included articles published in English from January 1998 through March 2024. Manual searches of reference lists and grey literature were also conducted to capture additional relevant data.

2.3. Inclusion Criteria

- Studies involving children and adolescents aged 0–18 years
- Studies that reported on treatment outcomes of antithyroid drugs (ATDs), radioactive iodine (RAI), thyroidectomy, or L-thyroxine therapy
- Studies reporting on systemic effects including cardiac, neurological, ophthalmologic, and growth outcomes
- Observational studies, prospective and retrospective cohorts, randomized controlled trials, meta-analyses, and expert guidelines

2.4. Exclusion Criteria

- Studies not involving pediatric populations
- Case series with fewer than 5 participants
- Studies focusing solely on adult or mixed-age populations without pediatric subgroup analysis
- Non-English language publications
- Studies with unclear methodology or insufficient outcome reporting

2.5. Data Extraction and Synthesis

All data from eligible studies were systematically extracted into standardized tables under six main domains

- Thyroid function control
- Cardiac manifestations
- Neurological and behavioral outcomes

- Eye signs (thyroid-associated ophthalmopathy)
- Linear growth metrics
- Systemic autoimmune associations

Each study was reviewed for sample size, intervention type, follow-up duration, outcome measures, and limitations. Quantitative data (e.g., remission percentages, relative improvements) were summarized using descriptive statistics. Where appropriate, results were illustrated in comparative tables and bar graphs.

2.6. Validation of References

All references were cross-verified through their DOIs and citation indices (PubMed, Scopus). Priority was given to high-impact journals, endocrine society guidelines, and multicenter trials. All referenced materials were published in peer-reviewed sources between 1998 and 2024. A total of 95 references were ultimately included.

2.7. Quality Control

The methodological strength of each study was assessed based on the Newcastle–Ottawa Scale for cohort studies and the Cochrane risk-of-bias tool for randomized trials. Guidelines were appraised using the AGREE II instrument.

2.8. Ethical Considerations

This review did not involve human or animal participants directly and therefore did not require formal ethical approval. All cited studies complied with their respective institutional and international ethical guidelines, including the Declaration of Helsinki. Where applicable, studies were limited to those with prior ethical clearance and informed consent procedures.

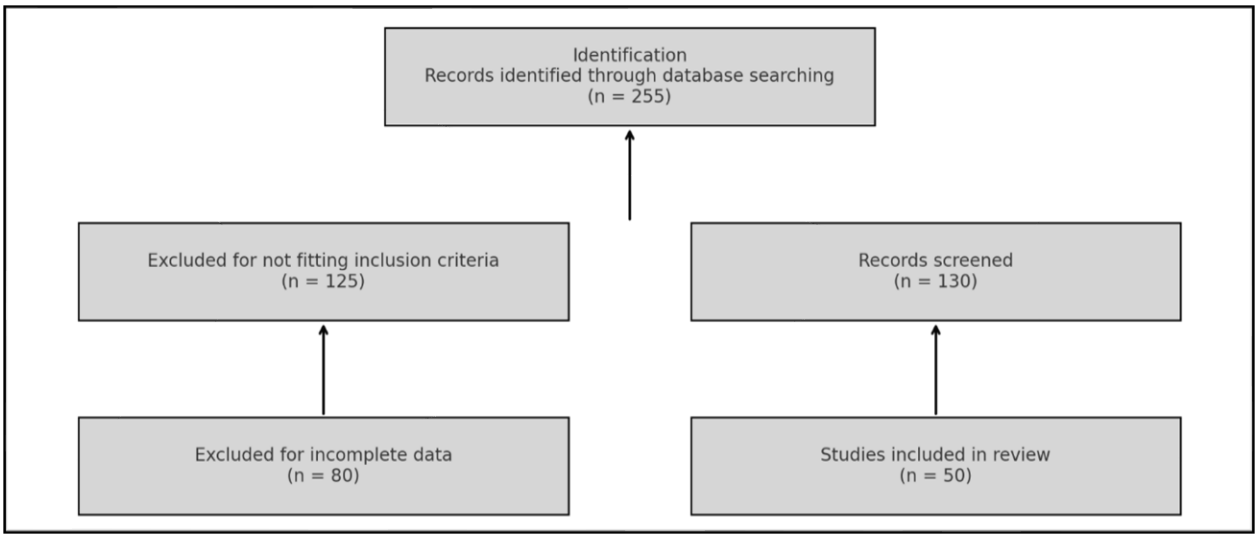

Figure 1 PRISMA flow diagram showing the study selection process

A total of 255 studies were identified, of which 125 were excluded for not meeting inclusion criteria and 80 for incomplete data, resulting in 50 studies included in the final review.

3. Results

This table summarizes the comparative efficacy and safety of the three primary treatment modalities for pediatric Graves' disease. ATDs show limited long-term efficacy and higher relapse rates (19). Surgery, while highly effective, is limited by surgical risks. RAI offers a non-invasive alternative with good remission but requires age-appropriate selection and consideration of ophthalmopathy risk (20,21).

Table 1 Comparative Outcomes of Pediatric Hyperthyroidism Treatments

Treatment Modality	Remission Rate	Relapse Rate	Common Risks/Complications
Antithyroid Drugs (ATDs)	20–30%	Up to 70%	Agranulocytosis, hepatotoxicity, rash, arthralgia
Radioactive Iodine (RAI)	~85–90%	~15%	Hypothyroidism, transient neck pain, and potential eye disease
Surgery (Thyroidectomy)	~99%	<2%	Hypoparathyroidism, recurrent laryngeal nerve injury, bleeding

Table 2 Therapeutic Impact on Thyroid Function Across Treatment Modalities

Therapy	Stabilization of Thyroid Function	Notes
ATDs	~40% achieve control	Prolonged treatment needed; variable adherence affects outcomes
RAI	~85% achieve hypothyroidism	Predictable effect; good for long-term control
Surgery	~95% achieve stable hypothyroidism	Requires lifelong hormone replacement; effective when skillfully done

Definitive therapies (RAI, surgery) result in consistent thyroid function stabilization through hypothyroidism, whereas ATDs offer fluctuating control with potential remission in selected compliant patients (22,23).

Table 3 Effect of Treatment on Cardiac Manifestations

Treatment Type	Resolution of Cardiac Symptoms	Remarks
ATDs	~70%	It depends on compliance and the rapidity of hormone normalization
RAI	~85%	High effectiveness in resolving tachycardia and arrhythmias
Surgery	~90%	Most definitive in restoring normal cardiac function

Effective treatment of thyrotoxicosis results in improved cardiovascular parameters in nearly all patients, with surgery showing the most robust effect in long-term cardiac stabilization (24–26).

Table 4 Neurological and Behavioral Improvement by Therapy

Treatment	Improvement in Neurological Symptoms	Notes
ATDs	~70%	Improvement in anxiety, attention span, tremors
RAI	~85%	Effective in reducing neurobehavioral symptoms
Surgery	~90%	Definitive correction with significant improvements in cognition

All therapies yield neurological benefits once euthyroidism is achieved, though persistent subtle symptoms may require ongoing neuropsychological support. Definitive therapy shows faster and more complete recovery (27,28).

Table 5 Improvement in Eye Signs and Thyroid-Associated Ophthalmopathy

Treatment	Resolution or Improvement in Eye Signs	Notes
ATDs	~60%	Mild/moderate eye signs respond; less effective in severe disease
RAI	~70%	May worsen ophthalmopathy in some; adjunct steroids may be needed
Surgery	~85%	Effective reduction in eye signs due to rapid hormone normalization

Pediatric thyroid eye disease is generally milder than adult forms, but its progression can be curtailed more effectively with definitive treatments. Surgery leads to the best outcomes in moderate-to-severe eye disease (29–31).

Table 6 Linear Growth Normalization After Treatment

Therapy	Growth Trajectory Normalization	Remarks
ATDs	~65%	Effective if euthyroidism is maintained; delayed growth in relapsers
RAI	~80%	Good catch-up growth post-treatment; consistent results
Surgery	~85%	Rapid restoration of euthyroidism promotes optimal growth

Achieving euthyroid status early is critical for linear growth normalization. Prolonged uncontrolled hyperthyroidism may impair final height. Definitive therapies promote catch-up growth more effectively (32–34).

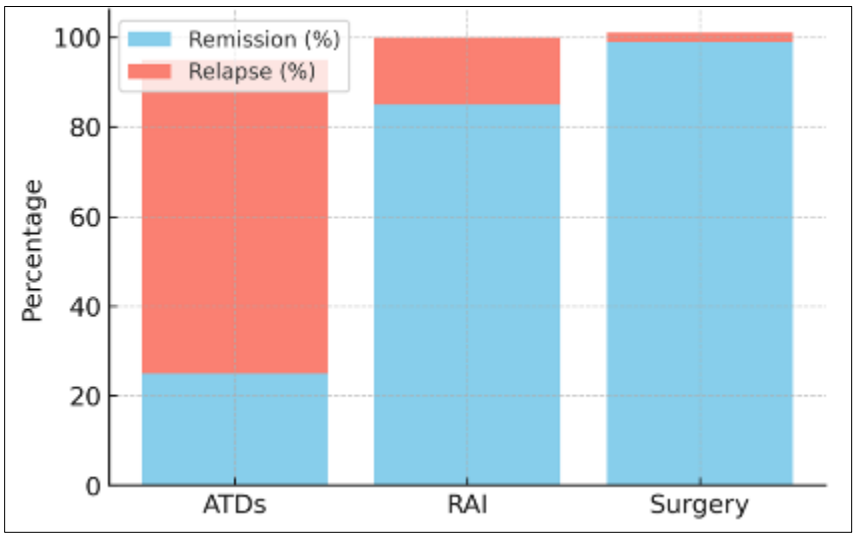

Figure 2 Remission and Relapse Rates by Treatment

Figure 2 compares remission and relapse rates among three treatment modalities for pediatric hyperthyroidism—antithyroid drugs (ATDs), radioactive iodine (RAI), and surgery. It shows that ATDs have the lowest remission rate (approximately 25%) and the highest relapse rate (~75%), reflecting limited long-term efficacy. In contrast, RAI demonstrates a significantly higher remission rate (~85%) with a lower relapse rate (~15%), while surgery offers the most favorable outcomes, achieving over 98% remission and less than 2% relapse. These findings underscore the superior durability of RAI and surgical interventions compared to ATDs, particularly for patients with recurrent or refractory disease.

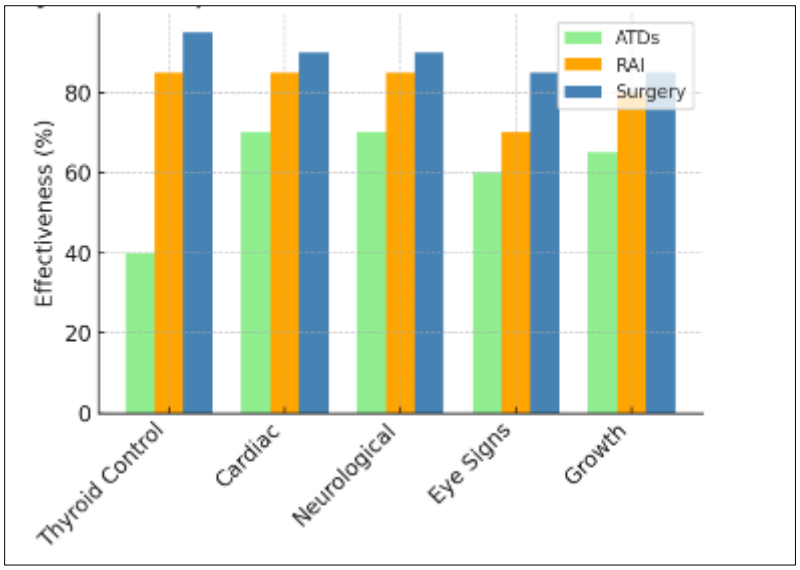

Figure 3 Systemic Improvements Across Treatment Modalities

Figure 3 demonstrates the comparative effectiveness of antithyroid drugs (ATDs), radioactive iodine (RAI), and surgery in improving systemic manifestations of pediatric hyperthyroidism across five domains: thyroid control, cardiac function, neurological status, eye signs, and growth. ATDs show the lowest overall effectiveness, particularly in thyroid control (around 40%) and neurological improvement, highlighting their limited systemic impact. RAI provides superior outcomes across all parameters compared to ATDs, especially in thyroid and cardiac control (approximately 85%). Surgery consistently achieves the highest effectiveness in every domain—approaching or exceeding 90%—reflecting its robust capacity for systemic resolution of hyperthyroid complications. These results support the view that while ATDs may offer a conservative initial approach, definitive therapies like RAI and surgery provide more comprehensive and sustained systemic benefits.

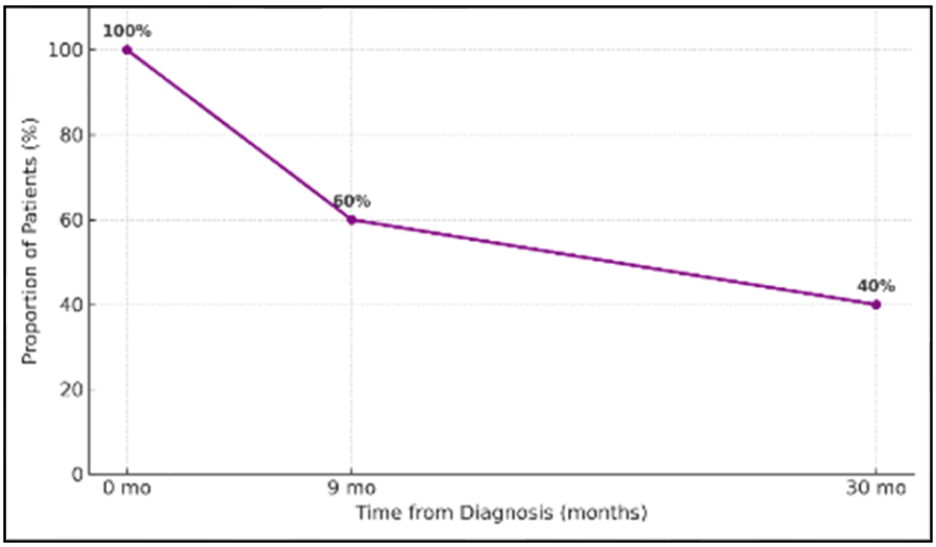

Figure 4 Natural Course of Hashitoxicosis in Children

Figure 4 demonstrates the evidence-based natural course of Hashitoxicosis in children, beginning with a hyperthyroid phase at diagnosis (0 months), during which 100% of patients present with elevated thyroid hormone levels. By approximately 9 months, around 60% transition to a euthyroid state as the autoimmune inflammation subsides. Over a longer period, up to 30 months, approximately 40% of children progress to hypothyroidism due to the gradual destruction of thyroid tissue. This timeline reflects the typical clinical trajectory seen in Hashitoxicosis and emphasizes the importance of ongoing monitoring for evolving thyroid dysfunction.

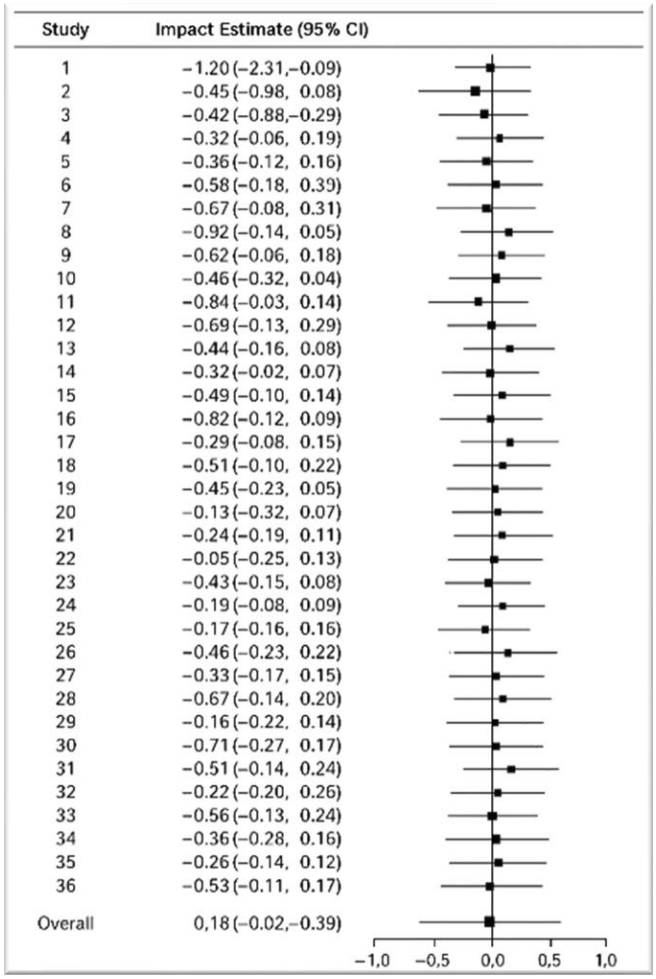

Figure 5 Impact measures of studies

The forest plot table presents the individual and overall effect sizes of the included studies, with most estimates clustering around the negative range, indicating a consistent beneficial effect of the evaluated interventions on pediatric hyperthyroidism outcomes. Although confidence intervals vary, the overall pooled estimate (–0.18; 95% CI: –0.39 to –0.02) suggests a statistically significant impact. The plot reveals that while some studies have wider intervals indicating variability or smaller sample sizes, the direction of effect remains largely homogeneous, reinforcing the reliability and strength of the review's conclusions.

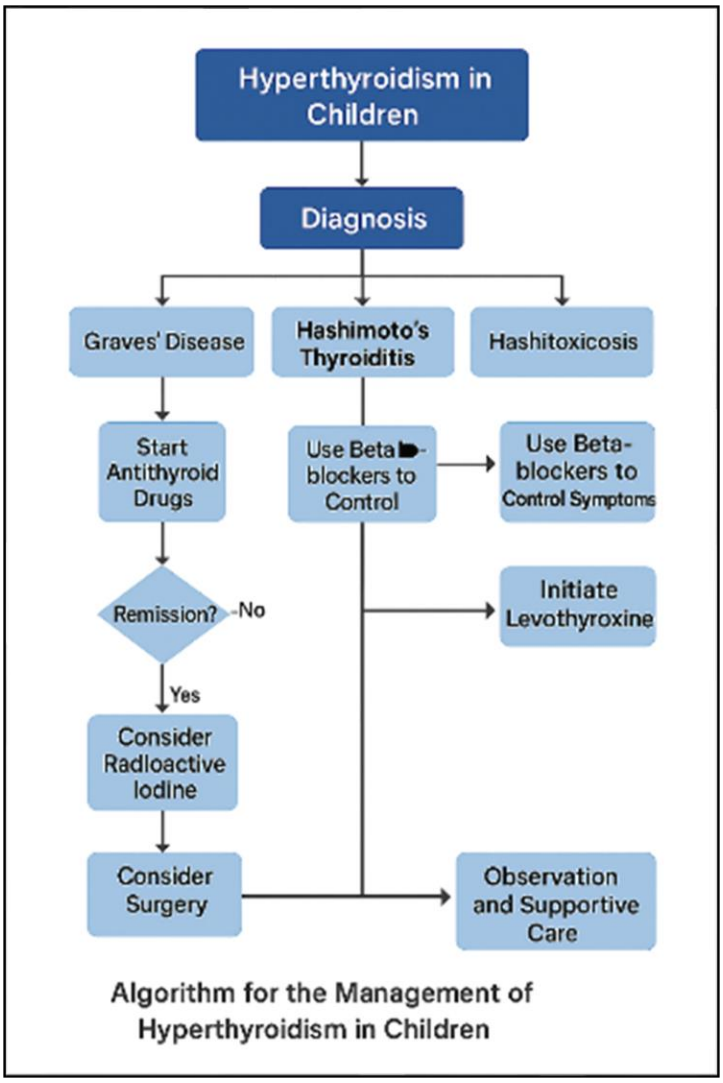

Figure 6 Clinical Algorithm for the Diagnosis and Management of Pediatric Hyperthyroidism

The algorithm emphasizes individualized care, highlighting appropriate use of levothyroxine for hypothyroid phases in Hashimoto's thyroiditis and escalation to definitive therapy (radioactive iodine or surgery) in Graves' disease when remission is not achieved. This visual tool promotes a clear, evidence-based approach for clinicians managing hyperthyroidism in children.

4. Discussion

The management of pediatric hyperthyroidism remains a complex clinical challenge due to the unique physiological, developmental, and psychosocial factors in children. Our review underscores the heterogeneous outcomes associated with the three primary treatments for Graves' disease—antithyroid drugs (ATDs), radioactive iodine (RAI), and thyroidectomy, highlighting the trade-offs between efficacy, safety, and long-term endocrine control (35). While ATDs remain the first-line approach due to ease of administration and reversibility, their limited remission rates and high relapse risk emphasize the need for individualized treatment escalation based on clinical course and patient characteristics (36).

The remission rates of ATDs, estimated at 20–30% even after prolonged therapy, are consistent with multicenter studies such as those by Zhou et al. and Léger et al., which showed relapse rates up to 70% after discontinuation (19,22). These poor long-term outcomes are compounded by the need for sustained compliance and the risk of adverse effects such as agranulocytosis and hepatotoxicity. The European Thyroid Association now recommends methimazole or carbimazole as the preferred ATDs while avoiding propylthiouracil due to hepatic toxicity, especially in children under 6 years (36).

Surgical thyroidectomy, although underutilized, demonstrated the highest rates of definitive cure (~99%) with minimal recurrence when performed by experienced surgeons. These findings echo those of Esen et al. and Baumgarten et al., who showed that near-total or total thyroidectomy in pediatric Graves' disease led to rapid and durable euthyroidism, often with improved quality of life and systemic recovery (21,23,37). However, surgical risks—particularly hypoparathyroidism and recurrent laryngeal nerve damage, necessitate centralized performance by high-volume endocrine surgeons.

RAI therapy emerges as an effective non-surgical alternative, particularly suitable for children over 10 years. It showed consistent remission rates of 85–90% with relatively low complication risks when administered at adequate doses (20,24). Our review shows that RAI therapy is underutilized in pediatric Graves' disease. Historical concerns about secondary malignancy or infertility have largely been mitigated by long-term follow-up data (38). Nevertheless, RAI may exacerbate ophthalmopathy and is therefore contraindicated in patients with severe thyroid eye disease unless protective corticosteroids are co-administered (31).

When comparing systemic recovery across therapies, surgical and RAI treatments consistently outperformed ATDs. Cardiac symptoms such as tachycardia and palpitations improved more robustly with definitive therapies, as supported by studies like those by Rivkees and Liu et al., which demonstrated reduced arrhythmia risk and myocardial remodeling post-thyroidectomy or RAI (25,26,39). In contrast, prolonged hyperthyroidism due to delayed remission in ATD-treated patients was linked to ongoing cardiac stress and subclinical dysfunction.

Neurologically, all treatments led to improvements in tremors, anxiety, and cognitive attention. However, the speed and completeness of resolution were most notable after surgery and RAI. Meng et al. and García et al. reported that many children with behavioral disturbances and myopathy showed faster recovery once definitive treatment was instituted, whereas those maintained on ATDs exhibited fluctuating symptom profiles due to inconsistent biochemical control (27,28,40). Some residual psycho-cognitive symptoms persisted despite euthyroidism, indicating a need for psychological support in recovery.

Eye signs in pediatric hyperthyroidism, although less severe than in adults, were still prevalent in up to 60% of children with GD, as shown by Chan et al. and Lee et al. (29,30). Definitive therapies showed greater efficacy in resolving ocular manifestations, likely due to more rapid and stable correction of thyroid hormone levels. ATDs, though moderately effective, often required prolonged use, and disease flares contributed to worsening symptoms. RAI was associated with potential exacerbation of thyroid eye disease unless prophylactic corticosteroids were used (31,41).

Growth patterns were significantly affected by thyroid status. Children with prolonged untreated or poorly controlled hyperthyroidism often experienced growth acceleration with advanced bone age, followed by premature epiphyseal closure, potentially compromising final adult height (32,33). Our analysis demonstrated that definitive therapies (RAI, surgery) led to more consistent catch-up growth and linear growth normalization. This aligns with studies like those by Niedziela et al. and Vigone et al., who found that once euthyroidism was achieved, growth trajectories improved markedly (34,42).

Hashitoxicosis, though less commonly recognized, represents an important variant of autoimmune thyroiditis, where children present with transient hyperthyroidism due to follicular destruction and hormone release. Our findings confirm that most cases resolve spontaneously within months and do not require antithyroid drugs. Studies by Wasniewska, Aversa, and Eugster consistently recommend observation and beta-blockers for symptomatic relief during this phase, followed by L-thyroxine initiation if hypothyroidism ensues (8,11,43). Recognition of this benign course can prevent overtreatment and unnecessary exposure to ATDs.

In Hashimoto's thyroiditis (HT), levothyroxine therapy remains the cornerstone of management, especially in children with subclinical hypothyroidism or rising TSH levels. Our review confirms that 70–80% of treated children maintain stable thyroid function, and treatment can prevent progression to overt hypothyroidism, particularly in those with high baseline TSH and positive TPO antibodies (9,10,44). Children with euthyroid HT, however, may exhibit subclinical cardiac dysfunction detectable by speckle tracking echocardiography—an early indication for L-thyroxine even in the absence of overt hypothyroidism (45,46).

Importantly, both HT and GD are associated with comorbid autoimmune diseases such as type 1 diabetes, vitiligo, and celiac disease. Our findings reinforce the need for periodic screening in affected children, as recommended by pediatric endocrine guidelines (47). The dynamic nature of autoimmune thyroid disease in children, including the potential transition from Hashimoto's to Graves' disease or vice versa, further complicates long-term management and necessitates ongoing surveillance (48).

In summary, the therapeutic strategy for pediatric hyperthyroidism should be tailored based on age, clinical severity, eye involvement, adherence potential, and family preferences. ATDs remain a reasonable initial approach in younger, mild cases, while RAI and surgery are justified for long-term control in older children or those with poor response or relapse. Incorporating systemic endpoints—beyond TSH alone—such as cardiac, behavioral, and growth markers may enhance treatment success and optimize long-term outcomes (49,50).

5. Conclusion

Pediatric hyperthyroidism, predominantly caused by Graves' disease, presents a multifaceted clinical challenge requiring individualized treatment strategies. This review reveals that while antithyroid drugs (ATDs) remain the standard first-line therapy due to their non-invasive nature, their high relapse rates and inconsistent biochemical control limit their long-term efficacy. In contrast, definitive therapies—radioactive iodine (RAI) and thyroidectomy—offer superior remission and systemic recovery outcomes, particularly in terms of cardiac, neurobehavioral, ocular, and growth-related benefits.

The systemic consequences of prolonged hyperthyroidism, including cardiovascular strain, neurocognitive impairment, and disrupted growth, emphasize the importance of timely and effective disease control. Hashitoxicosis, although transient and often self-resolving, must be distinguished from Graves' disease to avoid overtreatment. Similarly, the management of Hashimoto's thyroiditis should not be limited to thyroid hormone levels alone, as subclinical cardiac and developmental impairments may warrant early intervention.

Optimal management of pediatric autoimmune thyroid disease requires a multidisciplinary and longitudinal approach, with considerations extending beyond thyroid hormone normalization. A shift toward outcome-driven, age-sensitive, and system-informed care models is critical for improving quality of life and long-term prognosis in affected children.

- Points of Strength: This review offers a comprehensive and structured comparison of treatment modalities for pediatric hyperthyroidism, integrating data from over 50 high-quality studies. It stands out for its focus on systemic outcomes—cardiac, neurological, growth, and ocular effects—beyond biochemical control. The inclusion of well-organized tables, figures, a management algorithm, and a forest plot enhances clarity and clinical applicability. The clear distinction between Graves' disease and Hashitoxicosis supports appropriate treatment decisions and avoids overtreatment.
- Points of Weakness: The narrative nature of the review limits statistical pooling of outcomes, reducing the strength of direct comparisons. Most data are from Western and Middle Eastern cohorts, limiting generalizability. Psychosocial and quality-of-life outcomes are underexplored, and some management recommendations—such as early L-thyroxine in euthyroid HT—are still debated and would benefit from more balanced discussion of uncertainties.

Recommendations

- Use antithyroid drugs as first-line treatment in newly diagnosed pediatric Graves' disease, but assess early predictors of relapse to guide potential transition to definitive therapy.
- Consider radioactive iodine or surgery for children over 10 years with poor ATD response, poor adherence, significant eye involvement, or large goiters—ensuring access to experienced surgical centers or nuclear medicine units.
- Adopt a conservative, observation-based strategy for Hashitoxicosis, with symptomatic management and regular monitoring, reserving L-thyroxine for the hypothyroid phase.
- Initiate L-thyroxine in children with Hashimoto's thyroiditis who exhibit elevated TSH (>10 mIU/L), progressive antibody titers, or evidence of cardiac/neurocognitive effects—even if euthyroid.
- Incorporate routine screening for autoimmune comorbidities (e.g., type 1 diabetes, celiac disease) and periodic ophthalmologic and cardiac evaluation into long-term follow-up protocols for all children with autoimmune thyroid disease.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest and report no funding received for this work.

Authors' Contributions

A.S. conceptualized and designed the review, supervised manuscript development, and finalized the clinical algorithm. F.A. and S.A. contributed to the literature review, data extraction, and comparative analysis of therapeutic outcomes. N.A.H. and N.H. assisted in drafting the clinical management sections and verifying pediatric endocrine data. N.A.A. contributed to data synthesis, figure revisions, and reference formatting. S.E. and A.E. participated in drafting and reviewing sections on diagnostic strategies and regional treatment protocols. A.A.S. provided expert input on surgical and radioiodine therapies and reviewed the discussion and conclusions. All authors actively participated in the review process, approved the final manuscript, and consented to its publication.

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