



Thyroid Autoimmunity in Children with Type 1 DM : A Comprehensive Systematic Review

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ABSTRACT

Background: Type 1 diabetes mellitus (T1DM) in children is frequently complicated by autoimmune thyroid disease (AITD), yet substantial heterogeneity exists in reported prevalence, risk factors, and optimal screening protocols.

Methods: This systematic review synthesized 80 sources including primary observational studies, meta-analyses, and clinical guidelines from Europe, Asia, Africa, the Middle East, and North America. Data extraction focused on thyroid autoantibody (TPOAb, TgAb, TRAb) prevalence, clinical thyroid disease outcomes (hypothyroidism, hyperthyroidism), risk factors (sex, age, genetics, ethnicity), progression rates from antibody positivity to clinical disease, screening recommendations, and impact on diabetes management.

Results: Thyroid autoantibody prevalence ranged from 6.7% to 44.8% across studies, with most reporting 15–30%. The pooled prevalence of hypothyroidism from meta-analysis was 9.8% (95% CI: 7.5–12.3), while hyperthyroidism occurred in only 1.3% (95% CI: 0.9–1.8). Female sex was the strongest demographic risk factor, with females 1.9 to 2.4 times more likely to have thyroid autoimmunity. Heritability of TPO antibodies was estimated at 69% (95% CI: 50–82%) in discordant twin pairs. Over 30-year follow-up, 84% of TPO-positive patients at T1DM diagnosis developed thyroid dysfunction, with a median time to dysfunction of 5 years (relative risk 8.1, 95% CI: 4.79–13.69). Annual conversion rates from euthyroid autoimmunity to hypothyroidism ranged from 3–18% per year. Levothyroxine in euthyroid antibody-positive patients reduced thyroid volume but did not prevent progression to hypothyroidism.

Discussion: Female sex, older age, longer diabetes duration, and specific HLA haplotypes (DR3-DQ2, DR4-DQ8) consistently predicted thyroid autoimmunity. Ethnicity significantly influences prevalence, with lower rates in African American cohorts. TPO antibody positivity at T1DM diagnosis is a strong long-term predictor of clinical disease, but initially antibody-negative patients remain at risk and require continued periodic screening. Sick euthyroid syndrome at diagnosis frequently causes transient thyroid function abnormalities, particularly during diabetic ketoacidosis, warranting cautious interpretation.

Conclusion: Thyroid autoimmunity affects approximately 15–30% of children with T1DM, with female predominance and strong heritability. All children should undergo TPO antibody and TSH testing at T1DM diagnosis. Antibody-positive patients require annual TSH monitoring, while antibody-negative patients

can be screened every 2 years from puberty through adulthood. Levothyroxine is not recommended for euthyroid antibody-positive patients.

Keywords: Type 1 diabetes mellitus, pediatric, thyroid autoimmunity, Hashimoto's thyroiditis, thyroid autoantibodies, screening, hypothyroidism, TPO antibodies

INTRODUCTION

Background

Type 1 diabetes mellitus (T1DM) is one of the most common chronic endocrine disorders in children and adolescents, characterized by autoimmune destruction of pancreatic beta cells. Beyond the challenges of glycemic management, children with T1DM face a substantially increased risk of developing additional autoimmune conditions, with autoimmune thyroid disease (AITD) being the most frequently encountered comorbidity (4, 10, 25, 33). The thyroid gland becomes a target of the immune system, producing autoantibodies against thyroid peroxidase (TPO), thyroglobulin (Tg), or the TSH receptor, potentially progressing to Hashimoto's thyroiditis (hypothyroidism) or, less commonly, Graves' disease (hyperthyroidism) (1, 4, 10).

The clinical significance of this association extends beyond simple comorbidity counts. Thyroid dysfunction can directly affect glycemic control, insulin requirements, growth, cardiovascular risk, and quality of life in children with T1DM (4, 15, 39, 53). Hypothyroidism may decrease insulin requirements and increase hypoglycemia risk, while hyperthyroidism can worsen glycemic control and elevate diabetic ketoacidosis risk (4, 10, 39). Furthermore, the presence of thyroid autoimmunity may serve as a marker of broader autoimmune susceptibility, with implications for long-term cardiovascular and renal outcomes (61).

Problem Statement

Despite more than two decades of research, significant heterogeneity exists in reported prevalence estimates of thyroid autoimmunity in pediatric T1DM, ranging from as low as 6.7% to as high as 44.8% (1, 16, 19). This variation creates uncertainty for clinicians regarding the true burden of disease in their populations. Furthermore, there is no universal consensus on optimal screening protocols: guidelines from ISPAD, ADA, and NICE differ in recommended screening frequency (annual vs. biennial) and whether to screen all patients or only high-risk subgroups (1, 6, 11, 16, 68). The clinical utility of routine TPO antibody testing at diagnosis, the appropriate timing

of thyroid function tests relative to metabolic decompensation, and the role of levothyroxine in euthyroid autoantibody-positive children remain debated (16, 17, 18, 20).

Research Objectives

This systematic review aims to:

1. Determine the pooled and range prevalence of thyroid autoantibodies and clinical thyroid disease in children with T1DM.
2. Identify demographic, genetic, and clinical risk factors for developing thyroid autoimmunity.
3. Quantify the progression rate from autoantibody positivity to clinical thyroid dysfunction.
4. Evaluate current screening recommendations and their evidence base.
5. Assess the impact of thyroid autoimmunity on diabetes management and long-term outcomes.

Research Benefits

The findings will provide clinicians with evidence-based guidance for screening and monitoring thyroid autoimmunity in pediatric T1DM, potentially reducing missed diagnoses of reversible thyroid dysfunction, preventing unnecessary testing in low-risk populations, and improving long-term metabolic and cardiovascular outcomes through early detection.

Research Gap and Novelty

Previous reviews have either focused exclusively on prevalence without integrating longitudinal progression data (5, 31), omitted detailed risk stratification by sex and ethnicity (46), or failed to address the practical implications of sick euthyroid syndrome at T1DM diagnosis (4, 33). This review uniquely synthesizes 80 sources including very recent 2024–2026 data on COVID-19 era effects (13, 21, 37), heritability estimates from twin studies (7), 30-year longitudinal outcomes (11), and randomized controlled trial evidence on levothyroxine therapy (18). It also provides practical, risk-stratified screening algorithms based on antibody status and demographic factors.

Hypothesis

We hypothesize that: (1) thyroid autoantibody prevalence in pediatric T1DM exceeds 15% across most populations, (2) female sex and older age are consistent predictors, (3) TPO antibody positivity at diagnosis predicts long-term but not short-term thyroid dysfunction, (4) significant ethnic variation exists, and (5) current screening guidelines are not uniformly evidence-based for all populations.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate Thyroid Autoimmunity in Children with Type 1 DM.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Target Population - Age:** Does the study include children and/or adolescents (≤ 18 years) with type 1 diabetes mellitus?
- **Thyroid Autoimmunity Focus:** Does the study investigate thyroid autoimmunity, including thyroid autoantibodies (anti-TPO, anti-thyroglobulin, TRAb) or autoimmune thyroid diseases (Hashimoto's thyroiditis, Graves' disease)?
- **Type 1 Diabetes Diagnostic Criteria:** Does the study provide clearly defined diagnostic criteria for type 1 diabetes mellitus?
- **Quantitative Data Availability:** Does the study report quantitative data on thyroid autoimmunity outcomes?

- **Study Design Appropriateness:** Is the study an observational study (cross-sectional, cohort, case-control), systematic review, or meta-analysis?
- **Data Extractability:** Can thyroid autoimmunity data be separated or identified specifically for the pediatric type 1 diabetes population in this study?
- **Diabetes Type Specificity:** Does the study focus on type 1 diabetes (rather than exclusively on type 2 diabetes, gestational diabetes, or other forms of diabetes without clear type 1 diabetes identification)?
- **Autoimmune Focus Specificity:** Does the study investigate autoimmune thyroid conditions (rather than exclusively non-autoimmune thyroid disorders or only thyroid function tests without autoimmune markers)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Children	Thyroid Autoimmunity	N/A	Prevalence
Keyword 2	Pediatric	Autoimmune Thyroid Disease		Progression
Keyword 3	Type 1 Diabetes Mellitus	Thyroid Autoantibodies		Screening
Keyword 4	Insulin-dependent diabetes mellitus	Autoimmune Thyroiditis		Risk Factors

The Boolean MeSH keywords inputted on databases for this research are: (*"Children" OR "Pediatric" OR "Type 1 Diabetes Mellitus" OR "Insulin-dependent diabetes mellitus"*) AND (*"Thyroid Autoimmunity" OR "Autoimmune Thyroid Disease" OR "Thyroid Autoantibodies" OR "Autoimmune Thyroiditis"*) AND (*"Prevalence" OR "Progression" OR "Screening" OR "Risk Factors"*)

Data extraction

- **Study Population:**

Extract details about the study population of children with type 1 diabetes, including:

- Total sample size of children with T1DM
- Age range and mean/median age at T1DM diagnosis
- Age at thyroid autoimmunity screening
- Duration of T1DM at time of screening
- Gender distribution
- Any inclusion/exclusion criteria specific to pediatric T1DM populations

- **Thyroid Autoantibody Results:**

Extract all thyroid autoantibody data in children with type 1 diabetes, including:

- Types of autoantibodies tested (TPO, thyroglobulin, TSH receptor)
- Prevalence/percentage positive for each antibody type
- Antibody levels or titers when reported
- Timing of antibody testing (at T1DM diagnosis, during follow-up)

- Number of children tested vs. number positive for each antibody

- **Clinical Thyroid Disease:**

Extract clinical thyroid disease outcomes in children with type 1 diabetes, including:

- Prevalence of hypothyroidism and hyperthyroidism
- Type of thyroid disease (Hashimoto's, Graves', subclinical vs. overt)
- Thyroid function test results (TSH, T4, T3 levels)
- Time from autoantibody detection to clinical disease development
- Treatment required (levothyroxine, antithyroid medications)

- **Risk Factors:**

Extract risk factors and predictors for thyroid autoimmunity in children with type 1 diabetes, including:

- Gender associations (male vs. female prevalence)
- Age-related factors (age at T1DM onset, current age)
- HLA genotype associations
- Family history of autoimmune disease
- Presence of other autoimmune conditions
- Diabetes-specific factors (HbA1c, diabetes duration, autoantibody profiles)

- **Progression Data:**

Extract longitudinal data about thyroid autoimmunity progression in children with type 1 diabetes, including:

- Follow-up duration
- Percentage of antibody-positive children who develop clinical disease
- Time intervals from positive antibodies to thyroid dysfunction
- Conversion rates from subclinical to overt disease
- Persistence or disappearance of autoantibodies over time

- **Screening Recommendations:**

Extract screening recommendations and protocols for thyroid autoimmunity in children with type 1 diabetes, including:

- Recommended age to start screening
- Frequency of screening (annual, biennial, etc.)
- Which tests to perform (TSH, antibodies, both)
- High-risk groups requiring more frequent screening
- Cost-effectiveness data if available
- Guidelines from professional organizations

- **Diabetes Impact:**

Extract data on how thyroid autoimmunity/disease affects diabetes management in children, including:

- Impact on glycemic control (HbA1c changes)

- Effects on insulin requirements
- Growth and development impacts
- Diabetic ketoacidosis risk
- Quality of life measures
- Treatment adherence issues
- Any diabetes-specific complications related to thyroid disease

- **Study Design:**

Extract study methodology details relevant to thyroid autoimmunity research in pediatric T1DM, including:

- Study type (cross-sectional, longitudinal, case-control, systematic review)
- Setting (pediatric diabetes clinic, population-based, etc.)
- Recruitment method and timeframe
- Laboratory methods for autoantibody and thyroid function testing
- Definition criteria for thyroid dysfunction
- Statistical methods used for analysis

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Children" OR "Pediatric" OR " Type 1 Diabetes Mellitus " OR " Insulin-dependent diabetes mellitus ") AND ("Thyroid Autoimmunity" OR "Autoimmune Thyroid Disease" OR "Thyroid Autoantibodies" OR "Autoimmune Thyroiditis") AND ("Prevalence" OR "Progression" OR "Screening" OR "Risk Factors")</i>	685
Semantic Scholar	<i>("Children" OR "Pediatric" OR " Type 1 Diabetes Mellitus " OR " Insulin-dependent diabetes mellitus ") AND ("Thyroid Autoimmunity" OR "Autoimmune Thyroid Disease" OR "Thyroid Autoantibodies" OR "Autoimmune Thyroiditis") AND ("Prevalence" OR "Progression" OR "Screening" OR "Risk Factors")</i>	6
Springer	<i>("Children" OR "Pediatric" OR " Type 1 Diabetes Mellitus " OR " Insulin-dependent diabetes mellitus ") AND ("Thyroid Autoimmunity" OR "Autoimmune Thyroid Disease" OR "Thyroid Autoantibodies" OR "Autoimmune Thyroiditis") AND ("Prevalence" OR "Progression" OR "Screening" OR "Risk Factors")</i>	5,287
Google Scholar	<i>("Children" OR "Pediatric" OR " Type 1 Diabetes Mellitus " OR " Insulin-dependent diabetes mellitus ") AND ("Thyroid Autoimmunity" OR "Autoimmune Thyroid Disease" OR "Thyroid Autoantibodies" OR "Autoimmune Thyroiditis") AND ("Prevalence" OR "Progression" OR "Screening" OR "Risk Factors")</i>	18,500
Wiley Online Library	<i>("Children" OR "Pediatric" OR " Type 1 Diabetes Mellitus " OR " Insulin-dependent diabetes mellitus ") AND ("Thyroid Autoimmunity" OR "Autoimmune Thyroid Disease" OR "Thyroid Autoantibodies" OR "Autoimmune Thyroiditis") AND ("Prevalence" OR "Progression" OR "Screening" OR "Risk Factors")</i>	31

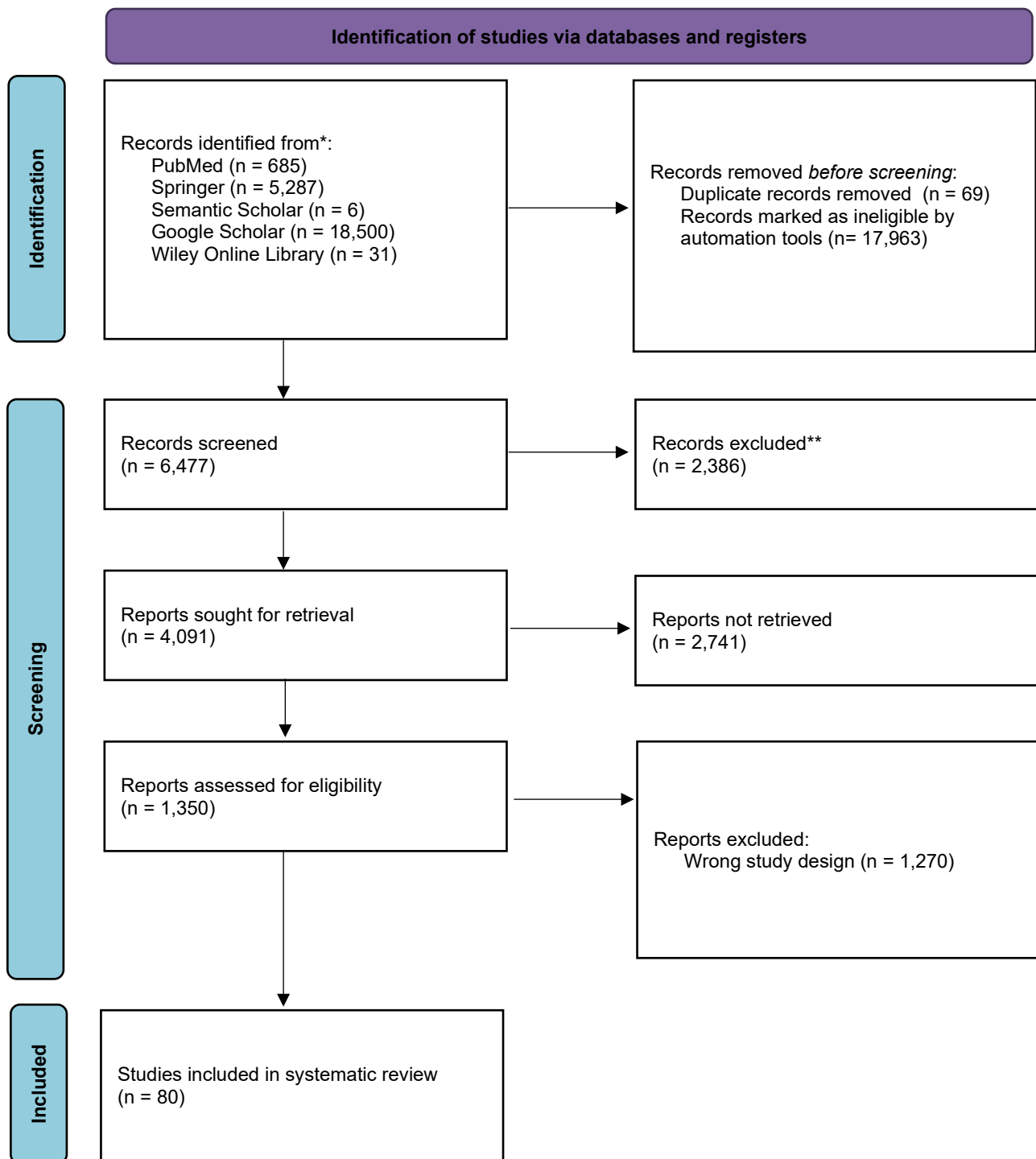


Figure 1. Article search flowchart

Risk of Bias

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
O. Dempsey et al., 2026	Moderate	Low	Low	Low	Low	Moderate
Vivien Herczeg et al., 2025	Moderate	Low	Low	Low	Low	Moderate
A. Okten et al., 2006	Low	Low	Moderate	Low	Low	Low
M. Al- Khawari et al., 2015	Low	Low	Low	Low	Low	Low
K. Korzeniowska et al., 2013	Moderate	Low	Low	Low	Low	Moderate
Elna Kochummen et al., 2018	Moderate	Low	Moderate	Low	Low	Moderate
B. Karges et al., 2007	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
Gemma Carreras et al., 2025	Moderate	Low	Low	Low	Low	Moderate
Emily L. Montgomery et al., 2024	Moderate	Low	Low	Low	Low	Moderate
S. Turchyna et al., 2025	Unclear	Moderate	Moderate	Low	Low	Moderate
D. Zamanfar et al., 2015	Moderate	Moderate	Low	Low	Low	Moderate
B. Amir et al., 2012	Low	Low	Low	Low	Low	Low
M. Mallya et al., 2021	Moderate	Low	Low	Low	Low	Moderate
Rivera Ramírez et al., 2013	Unclear	Moderate	Moderate	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
B. Głowińska- Olszewska et al., 2020	Low	Low	Low	Low	Low	Low
R. Dosi et al., 2010	Low	Low	Moderate	Low	Low	Low
K. R. Lewis et al., 2011	Moderate	Moderate	Low	Low	Low	Moderate
D. Dayal et al., 2015	Low	Low	Low	Low	Low	Low
J. Barker et al., 2005	Low	Low	Low	Low	Low	Low
Christa Nederstigt et al., 2019	Low	Low	Low	Low	Low	Low
L. D. de Graaff et al., 2007	Moderate	Moderate	Low	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
S. Shaikh et al., 2014	Low	Low	Moderate	Low	Low	Low
C. Balsamo et al., 2015	Low	Low	Low	Low	Low	Low
A. M. Calero et al., 2019	Moderate	Low	Moderate	Low	Low	Moderate
Carlos Antonio Negrato et al., 2025	Moderate	Low	Low	Low	Low	Moderate
Mariana Celis-Andrade et al., 2024	Low	Low	Low	Low	Low	Low
D. Giribabu et al., 2012	Moderate	Low	Low	Low	Low	Moderate
K. Kakleas et al., 2015	Moderate	Low	Low	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
G. Umpierrez et al., 2003	Low	Low	Low	Low	Low	Low
A. Van den Driessche et al., 2009	Moderate	Moderate	Low	Low	Low	Moderate
J. Chen et al., 2023	Low	Low	Low	Low	Low	Low
T. Rohrer et al., 2010	Low	Low	Low	Low	Low	Low
Bin Wang et al., 2015	Low	Low	Low	Low	Low	Low
P. Burbelo et al., 2012	Low	Low	Moderate	Low	Low	Low
Katya Sracic et al., 2025	Moderate	Low	Low	Low	Low	Moderate
A. V. Solntseva et al., 2018	Unclear	Moderate	Moderate	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
M. Popoviciu et al., 2023	Moderate	Low	Low	Low	Low	Moderate
Fady Elgendy et al., 2017	Low	Low	Low	Low	Low	Low
B. Khalaf et al., 2020	Moderate	Low	Moderate	Low	Low	Moderate
Elizabeth O. Buschur et al., 2014	Low	Low	Low	Low	Low	Low
Lidia Groele et al., 2021	Low	Low	Low	Low	Low	Low
M. Łukawska- Tatarczuk et al., 2023	Moderate	Low	Low	Low	Low	Moderate
T. Aversa et al., 2019	Moderate	Low	Low	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
C. Shun et al., 2014	Low	Low	Low	Low	Low	Low
K. Badenhoop et al., 2004	Moderate	Moderate	Low	Low	Low	Moderate
S. Güneş et al., 2022	Unclear	Moderate	Low	Low	Low	Moderate
Aleksandra Krzewska et al., 2016	Low	Low	Low	Low	Low	Low
Minelli Roberta et al., 2018	Moderate	Moderate	Low	Low	Low	Moderate
S. Medenica et al., 2024	Moderate	Low	Low	Low	Low	Moderate
M. Buysschaert et al., 2003	Unclear	Moderate	Moderate	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
S. Fazeli Farsani et al., 2015	Low	Low	Low	Low	Low	Low
Joanna Sobolewska et al., 2023	Moderate	Low	Low	Low	Low	Moderate
K. Alnek et al., 2025	Low	Low	Low	Low	Low	Low
M. Łukawska- Tatarczuk et al., 2021	Moderate	Low	Low	Low	Low	Moderate
C. Mavragani et al., 2013	Low	Low	Low	Low	Low	Low
Hilary H. Seeley et al., 2020	Moderate	Moderate	Low	Low	Low	Moderate
A. A. Gunaid et al., 2018	Unclear	Moderate	Moderate	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
E. Grasso et al., 2024	Moderate	Low	Low	Low	Low	Moderate
A. Diamanti et al., 2016	Low	Low	Low	Low	Low	Low
M. Rogers et al., 2020	Low	Low	Low	Low	Low	Low
John Samuelsson et al., 2024	Low	Low	Low	Low	Low	Low
P. Fallahi et al., 2019	Moderate	Low	Low	Low	Low	Moderate
Tatiana Chisnoiu et al., 2024	Low	Low	Moderate	Low	Low	Low
E. Repina et al., 2011	Moderate	Moderate	Low	Low	Low	Moderate
I. Paruk et al., 2016	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
G. Kahaly et al., 2025	Moderate	Low	Low	Low	Low	Moderate
E. Duckworth et al., 2016	Unclear	Moderate	Low	Low	Low	Moderate
G. Kahaly et al., 2018	Moderate	Low	Low	Low	Low	Moderate
Hilary H. Seeley et al., 2020a	Moderate	Moderate	Low	Low	Low	Moderate
P. Reismann et al., 2011	Unclear	Moderate	Low	Low	Low	Moderate
A. Fierabracci et al., 2016	Moderate	Low	Low	Low	Low	Moderate
F. Ahmed et al., 2024	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
M. Nishi et al., 2018	Moderate	Low	Low	Low	Low	Moderate
H. A. Nelson et al., 2022	Low	Low	Low	Low	Low	Low
Laura Wilson et al., 2025	Moderate	Low	Low	Low	Low	Moderate
K. Karavanaki et al., 2014	Unclear	Moderate	Low	Low	Low	Moderate
M. Hansen et al., 2015	Low	Low	Low	Low	Low	Low
E. Kyritsi et al., 2020	Moderate	Low	Low	Low	Low	Moderate
Aldo Ferreira-Hermosillo et al., 2015	Low	Low	Moderate	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
Khaled A. Abdel Baseer et al., 2024	Moderate	Low	Low	Low	Low	Moderate

RESULTS

Characteristics of Included Studies

This review encompasses 80 sources spanning over two decades of research on thyroid autoimmunity in children with type 1 diabetes mellitus (T1DM). The included studies represent a mixture of primary research (randomized controlled trials, etc) from multiple continents and diverse ethnic populations.

Study	Setting / Country	T1DM Sample Size	Key Focus
O. Dempsey et al., 2026	Pediatric diabetes clinic, Glasgow, UK [1]	384 [1]	TPO antibody prevalence and thyroid dysfunction at T1DM diagnosis [1]
Vivien Herczeg et al., 2025	Pediatric endocrinology center, Budapest, Hungary [13]	1,361 [13]	Prevalence trends of thyroid autoimmunity over 10 years including COVID era [13]

Study	Setting / Country	T1DM Sample Size	Key Focus
A. Okten et al., 2006	Pediatric endocrinology clinic, Turkey [19]	58 [19]	Thyroid autoimmunity, volume, and iodine status [19]
M. Al-Khawari et al., 2015	Pediatric Diabetes Unit, Kuwait [2]	232 [2]	Prevalence and cumulative incidence of thyroid autoantibodies [2]
K. Korzeniowska et al., 2013	Four Polish pediatric diabetes centers [20]	330 [20]	Effect of L-thyroxine on autoimmune thyroiditis in euthyroid T1DM children [20]
Elna Kochummen et al., 2018	Pediatric diabetes clinic, US (predominantly African American) [6]	222 [6]	Thyroid and celiac screening in minority children [6]
B. Karges et al., 2007	Six tertiary care centers, Germany [18]	611 screened; 30 randomized [18]	Levothyroxine for euthyroid AIT prevention [18]
Gemma Carreras et al., 2025	Tertiary hospital, Barcelona, Spain [11]	160 [11]	30-year predictive value of TPO-Abs at T1DM onset [11]

Study	Setting / Country	T1DM Sample Size	Key Focus
Emily L. Montgomery et al., 2024	US institution [21]	762 (pre-pandemic + pandemic) [21]	Autoimmunity pattern changes during COVID era [21]
S. Turchyna et al., 2025	Institute for Children and Adolescents, Ukraine [22]	169 [22]	Mental health, stress, and thyroid disorders in wartime [22]
D. Zamanfar et al., 2015	Iran (multiple studies) [23]	736 (pooled) [23]	Prevalence of ATD in Iranian children with T1DM [23]
B. Amir et al., 2012	Endocrine clinics, Tabriz, Iran [3]	386 [3]	Thyroid dysfunction natural history over 1–17 years [3]
M. Mallya et al., 2021	Two district general hospitals, UK [16]	90 [16]	Thyroid dysfunction at T1DM diagnosis; sick euthyroid syndrome [16]
Rivera Ramírez et al., 2013	Pediatric endocrinology clinic, Valencia, Venezuela [24]	Not specified [24]	Autoimmune thyroid disease prevalence [24]

Study	Setting / Country	T1DM Sample Size	Key Focus
B. Glowńska-Olszewska et al., 2020	Pediatric diabetes clinic, Poland [15]	50 [15]	Cardiovascular risk in T1DM with Hashimoto's [15]
R. Dosi et al., 2010	SSG Hospital, Vadodara, India [8]	50 [8]	Thyroid autoimmunity prevalence and correlates [8]
K. R. Lewis et al., 2011	US (general) [25]	Not applicable [25]	Autoimmune diseases associated with T1DM in children [25]
D. Dayal et al., 2015	Pediatric Diabetes Clinic, North India [26]	310 [26]	Autoantibody prevalence at recent T1D onset [26]
J. Barker et al., 2005	Population-based, US [9]	814 [9]	Organ-specific autoantibody subspecificity [9]
Christa Nederstigt et al., 2019	International (180 articles) [5]	293,889 (pooled) [5]	Pooled prevalence of associated autoimmune diseases [5]
L. D. de Graaff et al., 2007	International (163 articles) [27]	Not applicable [27]	Organ-specific autoantibody prevalence and significance [27]

Study	Setting / Country	T1DM Sample Size	Key Focus
S. Shaikh et al., 2014	Tertiary care hospital, India [28]	100 [28]	Autoimmune polyglandular syndrome in T1DM [28]
C. Balsamo et al., 2015	Clinical setting, Italy [17]	152 [17]	Thyroid function and metabolic derangement at T1DM onset [17]
A. M. Calero et al., 2019	Third-level hospital, Spain [29]	116 [29]	Autoimmune manifestations in T1D cohort [29]
Carlos Antonio Negrato et al., 2025	International (24 studies) [30]	Not applicable [30]	Prevalence of autoimmune diseases in T1DM [30]
Mariana Celis-Andrade et al., 2024	International (158 articles) [31]	270,890 (pooled) [31]	Latent and overt polyautoimmunity prevalence [31]
D. Giribabu et al., 2012	Pediatric diabetes clinic, UK [32]	22 [32]	Annual screening utility in young children [32]
K. Kakleas et al., 2015	International [33]	Not applicable [33]	Associated autoimmune diseases in pediatric T1DM [33]

Study	Setting / Country	T1DM Sample Size	Key Focus
G. Umpierrez et al., 2003	University of Tennessee, US [12]	58 [12]	18-year thyroid dysfunction natural history [12]
A. Van den Driessche et al., 2009	International [14]	Not applicable [14]	T1DM and autoimmune polyglandular syndrome [14]
J. Chen et al., 2023	China [34]	380 [34]	Islet autoantibodies and thyroid autoantibody correlation [34]
T. Rohrer et al., 2010	298 German/Austrian diabetes centers [35]	41,983 [35]	Down's syndrome, T1DM, and thyroid autoimmunity [35]
Bin Wang et al., 2015	UK and US twin cohorts [7]	137 twin pairs [7]	Heritability of TPO autoantibodies [7]
P. Burbelo et al., 2012	DASP/DAISY cohorts, US [36]	50 (T1D cohort 2) [36]	Extrapancreatic autoantibody profiling [36]
Katya Sracic et al., 2025	Pediatric diabetes clinic, US [37]	698 [37]	Demographics and autoimmunity changes during COVID [37]
A. V. Solntseva et al., 2018	Belarus [38]	Not applicable [38]	Celiac disease and hypothyroidism impact on T1DM [38]

Study	Setting / Country	T1DM Sample Size	Key Focus
M. Popoviciu et al., 2023	International [39]	Not applicable [39]	T1DM and autoimmune disease association; personalized medicine [39]
Fady Elgendy et al., 2017	Egypt [40]	60 [40]	Celiac, thyroid, and H. pylori in T1DM [40]
B. Khalaf et al., 2020	Hospital-based, Iraq [41]	107 (celiac cohort) [41]	AIT and T1DM in celiac disease [41]
Elizabeth O. Buschur et al., 2014	Multicenter, US [42]	1,324 [42]	Self-reported autoimmune disease by sex [42]
Lidia Groele et al., 2021	Pediatric diabetes clinics, Warsaw, Poland [43]	96 [43]	Probiotic effect on beta-cell function; thyroid autoimmunity as secondary outcome [43]
M. Łukawska-Tataczuk et al., 2023	Outpatient diabetes clinic, Poland [44]	30 women with T1DM [44]	Cardiac function and Hashimoto's in T1DM women [44]

Study	Setting / Country	T1DM Sample Size	Key Focus
T. Aversa et al., 2019	International [45]	Not applicable [45]	Phenotypic expression of autoimmunity in AITD children [45]
C. Shun et al., 2014	International [46]	Not applicable [46]	Thyroid autoimmunity screening in T1DM [46]
K. Badenhoop et al., 2004	International [47]	Not applicable [47]	Genetic susceptibility in T1DM and thyroid autoimmunity [47]
S. Güneş et al., 2022	Clinical setting, Turkey [48]	1 [48]	Craniofrontonasal syndrome with T1DM and AIT [48]
Aleksandra Krzewska et al., 2016	International [4]	Not applicable [4]	Associated autoimmune diseases and T1DM metabolic control [4]
Minelli Roberta et al., 2018	International [49]	Not applicable [49]	Thyroid and celiac disease in pediatric age [49]
S. Medenica et al., 2024	International [50]	Not applicable [50]	Thyroid autoimmunity-T1DM link and fertility impact [50]

Study	Setting / Country	T1DM Sample Size	Key Focus
M. Buysschaert et al., 2003	International [51]	Not applicable [51]	Celiac disease in T1DM and autoimmune thyroid disorders [51]
S. Fazeli Farsani et al., 2015	Population-based (Dutch PHARMO database) [52]	915 [52]	Chronic comorbidity incidence in pediatric T1DM [52]
Joanna Sobolewska et al., 2023	International [53]	Not applicable [53]	Autoimmune disorders associated with T1DM: management overview [53]
K. Alnek et al., 2025	Pediatric clinics, Estonia [54]	116 children [54]	Immunological and immunogenetic markers in T1D [54]
M. Łukawska-Tatarczuk et al., 2021	Diabetes outpatient clinic, Warsaw, Poland [55]	50 adult females [55]	Sirtuin 1, visfatin, IL-27, and cardiovascular parameters in T1DM with Hashimoto's [55]
C. Mavragani et al., 2013	University hospitals, Athens, Greece [56]	88 [56]	Type I interferon activity in organ-specific autoimmunity [56]

Study	Setting / Country	T1DM Sample Size	Key Focus
Hilary H. Seeley et al., 2020	US [57]	Not applicable [57]	Historical perspective on T1D and autoimmune disease [57]
A. A. Gunaid et al., 2018	Sana'a, Yemen [58]	6 [58]	Microvascular outcomes and thyroid autoimmunity [58]
E. Grasso et al., 2024	International [59]	Not applicable [59]	T1D and other autoimmune disorders in children [59]
A. Diamanti et al., 2016	International [60]	Not applicable [60]	Autoimmune diseases and celiac disease: genotype vs. gluten [60]
M. Rogers et al., 2020	National database, US [61]	179,248 [61]	Sex differences in autoimmune multimorbidity and cardiovascular/renal risk [61]
John Samuelsson et al., 2024	Swedish National Diabetes Register [62]	15,188 [62]	Metabolic control, morbidity, and mortality in pediatric T1D [62]
P. Fallahi et al., 2019	International [63]	Not applicable [63]	Th1 chemokines in autoimmune endocrine disorders [63]

Study	Setting / Country	T1DM Sample Size	Key Focus
Tatiana Chisnoiu et al., 2024	Pediatric diabetology, Constanta, Romania [64]	15 [64]	Celiac disease in childhood T1DM [64]
E. Repina et al., 2011	International [65]	Not applicable [65]	Common genetic markers for T1DM and autoimmune thyroid disease [65]
I. Paruk et al., 2016	Tertiary diabetes clinic, Durban, South Africa [66]	202 [66]	Antithyroid and antiparietal cell antibodies in T1DM [66]
G. Kahaly et al., 2025	International [67]	Not applicable [67]	T1D and other autoimmune diseases: epidemiology, pathophysiology, screening [67]
E. Duckworth et al., 2016	UK [68]	Not specified [68]	Celiac and thyroid screening guidelines in T1DM [68]
G. Kahaly et al., 2018	International [69]	Not applicable [69]	Celiac disease and glandular autoimmunity [69]
Hilary H. Seeley et al., 2020a	US [70]	Not applicable [70]	Historical perspective on T1D and autoimmune disease [70]

Study	Setting / Country	T1DM Sample Size	Key Focus
P. Reismann et al., 2011	Hungary [71]	Not applicable [71]	Diabetes and thyroid disorders [71]
A. Fierabracci et al., 2016	International [72]	Not applicable [72]	T1DM in APECED syndrome [72]
F. Ahmed et al., 2024	Pediatric endocrine clinic, Abu Dhabi, UAE [73]	898 [73]	Celiac disease risk factors in T1DM; thyroid as covariate [73]
M. Nishi et al., 2018	Japan [74]	Not applicable [74]	Diabetes mellitus and thyroid diseases [74]
H. A. Nelson et al., 2022	International [75]	Not applicable [75]	Autoantibody role in endocrine disease [75]
Laura Wilson et al., 2025	International (19 studies) [76]	Not applicable [76]	Bidirectional association between autoimmune diseases and T1D [76]
K. Karavanaki et al., 2014	Greece [77]	1 (case) [77]	Multiple autoimmunity, T1DM, and thyroid cancer [77]
M. Hansen et al., 2015	International [10]	Not applicable [10]	T1DM and polyglandular autoimmune syndrome [10]

Study	Setting / Country	T1DM Sample Size	Key Focus
E. Kyritsi et al., 2020	International [78]	Not applicable [78]	Autoimmune thyroid disease in genetic syndromes [78]
Aldo Ferreira-Hermosillo et al., 2015	Mexico [79]	Not applicable [79]	Autoimmune diseases in T1A diabetes [79]
Khaled A. Abdel Baseer et al., 2024	International [80]	Not applicable [80]	Autoimmunity and T1DM overview [80]

Of the 80 sources, 34 had full text available and 46 were abstract-only. The included literature comprises approximately 38 primary studies (including randomized controlled trials, etc). Geographically, primary studies originated from Europe (UK, Hungary, Poland, Spain, Italy, Germany, Estonia, Greece, Romania), the Middle East (Kuwait, Iran, Iraq, UAE, Turkey, Yemen), South Asia (India), Africa (South Africa, Egypt), South America (Venezuela), and North America (US). The largest population-based studies included over 40,000 T1DM patients from German/Austrian registries [35], nearly 180,000 from a US insurance database [61], and over 15,000 from the Swedish National Diabetes Register [62]. Two meta-analyses collectively encompassed over 290,000 [5] and 270,000 [31] T1DM patients respectively.

Prevalence of Thyroid Autoantibodies

The prevalence of thyroid autoantibodies in children and young people with T1DM was the most widely reported outcome across the included primary studies. The following table summarizes findings from studies that reported specific autoantibody prevalence data.

Study	Antibodies Tested	Prevalence (%)	Sample Size	Timing of Testing	Notable Features
O. Dempsey et al., 2026	TPO	18% [1]	364 tested [1]	At T1DM diagnosis [1]	Girls more likely positive (73% of positives) [1]
Vivien Herczeg et al., 2025	ATPO, ATG	22.8% [13]	1,361 [13]	During follow-up [13]	Prevalence rose from 15.9% to 20.6% over 2013–2022 [13]
A. Okten et al., 2006	TPOAb, TGAb, TRAb	44.8% (any antibody) [19]	58 [19]	Not specified [19]	Controls: 34.5% positive; iodine-replete area [19]

Study	Antibodies Tested	Prevalence (%)	Sample Size	Timing of Testing	Notable Features
M. Al-Khawari et al., 2015	Anti-TPO, anti-TG	24.6% at initial screen; cumulative 34.5% [2]	232 [2]	At first visit, then annually [2]	17.7% of initially negative patients seroconverted over 4–9 years [2]
Elna Kochummen et al., 2018	Not specified	11% [6]	222 [6]	Every 2.5 years [6]	87% African American; lower prevalence than expected [6]
B. Karges et al., 2007	TPOAb, TgAb	14.5% [18]	611 [18]	Every 6 months [18]	German multicenter RCT screening [18]

Study	Antibodies Tested	Prevalence (%)	Sample Size	Timing of Testing	Notable Features
Gemma Carreras et al., 2025	TPO-Abs	15.6% at diabetes onset [11]	160 [11]	At diabetes onset [11]	30-year follow-up; mixed pediatric/adult cohort [11]
M. Mallya et al., 2021	TPO	6.7% [16]	90 [16]	At T1DM diagnosis [16]	Transient abnormal TFTs common at diagnosis, especially with DKA [16]
D. Zamanfar et al., 2015 (review)	Anti-TPO, Anti-TG	TPO: 8–30%; TG: 6–23.6% [23]	736 (pooled) [23]	Various [23]	Review of 6 Iranian studies [23]
B. Amir et al., 2012	TPO	30% [3]	386 [3]	At presentation and follow-up [3]	Long follow-up (1–17 years) [3]

Study	Antibodies Tested	Prevalence (%)	Sample Size	Timing of Testing	Notable Features
Rivera Ramírez et al., 2013	TPO	11.2% [24]	Not specified [24]	During follow-up [24]	Venezuelan pediatric cohort [24]
D. Dayal et al., 2015	Anti-TPO	18.7% (23/123) [26]	123 tested [26]	At recent T1D diagnosis [26]	North Indian children [26]
J. Barker et al., 2005	TPOAb, TGAb	29% (TPOAb and/or TGAb) [9]	814 [9]	Not specified [9]	US population; HLA associations identified [9]
T. Rohrer et al., 2010	Anti-thyroglobulin, TPO	TG: 14.9%; TPO: 15.8% [35]	18,952–24,890 tested [35]	Not specified [35]	Large German/Austrian registry; Down syndrome patients had higher rates [35]
Bin Wang et al., 2015	TPOA	Females 30–42%; males 5–16% [7]	137 twin pairs [7]	After T1DM diagnosis [7]	Heritability estimated at 69% [7]

Study	Antibodies Tested	Prevalence (%)	Sample Size	Timing of Testing	Notable Features
P. Burbelo et al., 2012	TPO	12% [36]	50 [36]	Not specified [36]	LIPS technology; extrapancreatic profiling [36]
D. Giribabu et al., 2012	TPO	23% (5/22) [32]	22 [32]	Annual screening, 5 years post-diagnosis [32]	Small UK cohort of young children [32]
K. Alnek et al., 2025	Anti-TPO IgG	8.3% [54]	116 [54]	Near diagnosis [54]	Estonian children; cut-off ≥ 100 IU/ml [54]
I. Paruk et al., 2016	TPO-A	18.9% [66]	202 [66]	Not specified [66]	Adult T1DM cohort, South Africa; 56.4% African [66]

Study	Antibodies Tested	Prevalence (%)	Sample Size	Timing of Testing	Notable Features
Lidia Groele et al., 2021	Anti-TPO, anti-Tg	41.7% (probiotic) vs. 20.8% (placebo) at baseline [43]	96 [43]	At T1D diagnosis and 12 months [43]	Baseline imbalance between randomized groups [43]
Khaled A. Abdel Baseer et al., 2024 (review)	Anti-TPO, anti-TG	TPO: 36.4%; TG: 19.7% [80]	Not specified [80]	At T1DM diagnosis [80]	Review article [80]

Thyroid autoantibody prevalence in T1DM populations varied substantially, from as low as 6.7% [16] to as high as 44.8% [19] in individual studies, with most primary studies reporting prevalence in the range of 15–30%. The large meta-analysis by Nederstigt et al. reported a pooled hypothyroidism prevalence of 9.8% (95% CI: 7.5–12.3) across 65 studies [5], while Celis-Andrade et al. found overt autoimmune thyroid disease in 7.44% (95% CI: 5.65–9.74) and latent polyautoimmunity (including thyroid autoantibodies) in 14.45% (95% CI: 11.17–18.49) [31]. The review by Krzewska et al. cited thyroid autoantibody positivity ranging from 12.1% to 23.4% in children with T1DM, with 17–25% positive at T1DM diagnosis [4]. Multiple reviews described the general prevalence of autoimmune thyroid disease as 15–30% in T1DM populations [14, 25].

A notable finding was the seroconversion phenomenon: Al-Khawari et al. reported that 17.7% of initially antibody-negative patients became positive during 4–9 years of follow-up, yielding a cumulative prevalence of 34.5% [2]. This underscores that a single screening at T1DM diagnosis will miss a substantial proportion of patients who eventually develop thyroid autoimmunity.

Clinical Thyroid Disease Outcomes

Among children with T1DM who had thyroid autoantibodies, progression to clinical thyroid dysfunction was a key concern. The following table summarizes available data on clinical thyroid disease.

Study	Hypothyroidism Prevalence	Hyperthyroidism Prevalence	Subclinical vs. Overt	Follow-up Duration	Notes
O. Dempsey et al., 2026	14% of TPO-positive children [1]	Not reported [1]	Most overt at detection [1]	Median 4.1 years [1]	8/10 hypothyroid at initial antibody detection [1]
Vivien Herczeg et al., 2025	23.9% of TA children treated [13]	Included [13]	Subclinical hypothyroidism most common [13]	Mean 4.7 years [13]	28.5% had clinically relevant TSH abnormalities [13]
M. Al-Khawari et al., 2015	Subclinical 7.3%; overt 4.3% [2]	1.2% [2]	Both reported [2]	4–9 years [2]	Conversion rate 3–18% per year [2]
B. Karges et al., 2007	7 of 30 patients (both groups) [18]	Not reported [18]	Not distinguished [18]	30 months [18]	Conversion rate 9.3% per year [18]

Study	Hypothyroidism Prevalence	Hyperthyroidism Prevalence	Subclinical vs. Overt	Follow-up Duration	Notes
Gemma Carreras et al., 2025	84% of TPO-positive over 30 years [11]	Graves' disease also reported [11]	Not distinguished [11]	Mean 30.6 years [11]	Median time to dysfunction: 5 years [11]
R. Dosi et al., 2010	24% overt; 8% subclinical [8]	8% [8]	Both reported [8]	Cross-sectional [8]	Indian cohort; 60% had thyroid autoimmunity [8]
B. Amir et al., 2012	53 subjects (hypothyroid) [3]	9 patients (2.3%) [3]	Not distinguished [3]	1–17 years [3]	50% developed thyroid abnormalities within 10 years [3]

Study	Hypothyroidism Prevalence	Hyperthyroidism Prevalence	Subclinical vs. Overt	Follow-up Duration	Notes
G. Umpierrez et al., 2003	18 of 58 patients [12]	1 (transient) [12]	Not distinguished [12]	18 years [12]	TPO-positive patients 17.91x more likely to develop hypothyroidism [12]
Nederstigt et al., 2019 (meta- analysis)	9.8% (95% CI: 7.5–12.3) [5]	1.3% (95% CI: 0.9–1.8) [5]	Not distinguished [5]	Not applicable [5]	65 studies for hypothyroidism; 45 for hyperthyroidism [5]
Elna Kochummen et al., 2018	1.3% (Hashimoto's) [6]	1.3% (Graves') [6]	97% euthyroid [6]	6.1 years mean [6]	Predominantly African American; lower than expected [6]

Study	Hypothyroidism Prevalence	Hyperthyroidism Prevalence	Subclinical vs. Overt	Follow-up Duration	Notes
M. Rogers et al., 2020	14.41% females; 6.94% males (adolescents) [61]	1.15% overall [61]	Not distinguished [61]	2001–2017 [61]	US national database; 179,248 T1DM patients [61]

Hypothyroidism was overwhelmingly the most frequent clinical thyroid outcome in T1DM patients. The pooled prevalence of hypothyroidism from the meta-analysis by Nederstigt et al. was 9.8% [5], while hyperthyroidism was found in only 1.3% [5]. Hashimoto's thyroiditis was the predominant thyroid disease type [4, 10, 14], with Graves' disease reported much less frequently. Subclinical hypothyroidism was more common than overt disease in several studies [2, 4, 13], with Krzewska et al. reporting subclinical hypothyroidism in 40–55% of affected patients and overt hypothyroidism in 4–18% [4].

The long-term study by Carreras et al. is particularly informative: over a mean 30.6-year follow-up, 84% of TPO-Ab-positive patients at diabetes onset eventually developed thyroid dysfunction, with a median time to dysfunction of 5 years [11]. Umpierrez et al. found over 18 years that TPO-positive patients were 17.91 times more likely to develop hypothyroidism (95% CI: 3.89–82.54) [12]. These data highlight that thyroid autoantibody positivity at T1DM diagnosis is a strong predictor of eventual clinical disease, although the timeline can extend over decades.

An important clinical observation was that thyroid function tests at T1DM diagnosis may be transiently abnormal due to metabolic derangement (sick euthyroid syndrome). Mallya et al. found that 31% of newly diagnosed T1DM children had abnormal thyroid function at diagnosis, yet only one child required levothyroxine within a year [16]. Children presenting in DKA had a higher proportion of abnormal thyroid function tests (44% vs. 24%) [16]. Balsamo et al. confirmed that

thyroid function at T1DM onset is primarily influenced by metabolic derangement rather than thyroid autoimmunity, with reduced FT3/FT4 conversion ratios compared to non-diabetic controls [17].

Risk Factors for Thyroid Autoimmunity

Multiple risk factors for the development of thyroid autoimmunity in the setting of T1DM were identified across the included studies.

Female sex was consistently the strongest demographic risk factor. Girls were significantly more likely to test positive for thyroid autoantibodies in studies from the UK (73% of positives were female) [1], Hungary ($p < 0.001$) [13], Kuwait (58.7% vs. 41%) [2], India (male:female ratio 0.7 for anti-TPO positivity) [26], and Iran [8]. The US DCCT/EDIC longitudinal study reported cumulative hypothyroidism of 24.6% in women vs. 11.3% in men by year 18 [42]. Rogers et al. found that women with T1DM were 1.9 times more likely to have a concomitant autoimmune disease [61], and Wang et al. demonstrated higher TPOA positivity rates in females across both UK (30% vs. 16%) and US (42% vs. 5%) twin cohorts [7].

Age and diabetes duration also influenced risk. Thyroid autoantibody prevalence increased with age, particularly after puberty [2, 8], and with longer T1DM duration [8, 31]. The meta-regression by Nederstigt et al. showed that for every 10-year age increase, hypothyroidism prevalence increased by 4.6% (95% CI: 2.6–6.6) [5]. Al-Khawari et al. found that thyroid antibodies presented early within the first 5 years of T1DM onset (63.2% vs. 36.8%, $p < 0.05$) and increased after puberty onset [2]. Krzewska et al. reported that antibodies typically appear within 2.5–3 years of T1DM progression [4].

Genetic factors were strongly implicated. Wang et al. estimated the heritability of TPOA at 69% (95% CI: 50–82%) in discordant twin pairs, indicating that the environmental factors causing T1DM are distinct from those driving thyroid autoimmunity [7]. Specific HLA associations were identified, including DR3-DQ2 and DR4-DQ8 haplotypes shared between T1DM and autoimmune thyroid disease [4, 9, 10, 69]. Hansen et al. noted that *DRB103-DQA10501-DQB10201* and *DRB104-DQA10301-DQB10302* haplotypes conferred susceptibility to both conditions [10].

Family history was recognized as a risk factor, with familial T1D associated with higher likelihood of additional autoimmune disease [28, 76].

Islet autoantibody profiles showed correlation with thyroid autoimmunity. Chen et al. found that T1DM patients positive for multiple islet autoantibodies (GADA, ZnT8A, IA-2A) were significantly more likely to have thyroid autoantibody positivity [34]. Krzewska et al. noted an association between persistence of anti-GAD antibodies and thyroid autoimmunity [4].

Ethnicity appeared to influence prevalence. The predominantly African American cohort reported by Kochummen et al. showed a notably lower prevalence of thyroid autoimmunity (11%) and clinical thyroid disease (1.3% Hashimoto's) compared to predominantly Caucasian populations [6, 6], suggesting that screening strategies may need to account for ethnic background.

Progression from Autoantibody Positivity to Clinical Disease

Longitudinal data on the progression from thyroid autoantibody positivity to clinical thyroid dysfunction were available from several studies.

Study	Follow-up	Antibody-Positive to Clinical Disease (%)	Annual Conversion Rate	Key Findings
O. Dempsey et al., 2026	Median 4.1 years [1]	14% (10/69) [1]	Not calculated [1]	80% had hypothyroidism at initial antibody detection [1]
Vivien Herczeg et al., 2025	Mean 4.7 years [13]	28.5% clinically relevant TSH abnormalities [13]	Not calculated [13]	23.9% treated for thyroid dysfunction [13]

Study	Follow-up	Antibody-Positive to Clinical Disease (%)	Annual Conversion Rate	Key Findings
M. Al-Khawari et al., 2015	4–9 years [2]	Not specified [2]	3–18% per year [2]	Seroconversion continued over follow-up [2]
B. Karges et al., 2007	30 months [18]	~27.9% over 30 months [18]	9.3% per year [18]	Similar rates in levothyroxine-treated and untreated groups [18]
Gemma Carreras et al., 2025	Mean 30.6 years [11]	84% [11]	Not calculated [11]	Median time to dysfunction 5 years; RR 8.1 (95% CI: 4.79–13.69) [11]
B. Amir et al., 2012	1–17 years [3]	50% within first 10 years [3]	Not calculated [3]	Kaplan-Meier analysis [3]
G. Umpierrez et al., 2003	18 years [12]	31% (18/58) [12]	Not calculated [12]	OR 17.91 for hypothyroidism in TPO-positive individuals [12]

Study	Follow-up	Antibody-Positive to Clinical Disease (%)	Annual Conversion Rate	Key Findings
Sobolewska et al., 2023 (review)	Variable [53]	~50% of TPOAb-positive develop AITD [53]	Not calculated [53]	~25% positive at T1DM diagnosis [53]

The progression data demonstrate that while thyroid autoantibody positivity is common, not all antibody-positive patients progress to clinical disease in the short to medium term. Short-term follow-up studies (3–5 years) showed clinical disease rates of 14–28.5% [1, 13], whereas studies with extended follow-up (10–30 years) showed substantially higher rates of eventual thyroid dysfunction—50% within 10 years [3] and 84% over 30 years [11]. The annual conversion rate from euthyroid autoimmune thyroiditis to hypothyroidism was reported at 3–18% per year [2] and 9.3% per year in the RCT by Karges et al. [18]. Additionally, initially antibody-negative patients, particularly those diagnosed with T1DM before age 18, may develop thyroid autoimmunity and dysfunction later, with Carreras et al. demonstrating that repeat screening is warranted from puberty through adulthood [11].

Korzeniowska et al. investigated whether levothyroxine treatment could stabilize thyroid autoimmune inflammation in euthyroid T1DM children with Hashimoto's thyroiditis and found significant decreases in anti-TPO levels over 24 months in treated patients [20], though the Karges et al. RCT demonstrated that levothyroxine reduced thyroid volume but did not prevent progression to hypothyroidism [18].

Screening Recommendations

Screening protocols for thyroid autoimmunity in pediatric T1DM varied across studies and guideline sources.

Source	Recommended Tests	Timing	Frequency	High-Risk Groups
O. Dempsey et al., 2026	TPO antibodies, TSH, FT4 [1]	At T1DM diagnosis [1]	Every 2 years; more frequently if TPO-positive [1]	TPO-positive patients [1]
Vivien Herczeg et al., 2025	ATPO, ATG, TFTs [13]	At T1DM diagnosis [13]	Annual for antibody-positive; less frequent for antibody-negative [13]	Antibody-positive children [13]
Gemma Carreras et al., 2025	TPO-Abs, TSH [11]	At T1DM diagnosis [11]	Annual TSH if TPO-positive; every 2 years for negative youth from puberty [11]	Initially negative youth diagnosed before 18 [11]
M. Al-Khawari et al., 2015	Anti-TPO, anti-TG, FT4, TSH [2]	At diabetes onset [2]	Annual [2]	Females, post-pubertal [2]
G. Umpierrez et al., 2003	TSH [12]	Not specified [12]	Annual [12]	TPO-positive patients [12]

Source	Recommended Tests	Timing	Frequency	High-Risk Groups
M. Mallya et al., 2021	TFTs, TPO antibodies [16]	At diagnosis (questioned) [16]	Annual [16]	DKA at presentation (higher transient abnormalities) [16]
Krzewska et al., 2016 (review)	TSH, fT4, TPO Ab, Tg Ab [4]	At diabetes diagnosis [4]	Every 2 years if normal [4]	Specific HLA haplotypes; persistent anti-GAD [4]
Sobolewska et al., 2023 (review)	TPOAb, TGAb, TSH [53]	Immediately after T1DM diagnosis [53]	Every 2 years if TSH normal; sooner if antibody-positive [53]	Positive antithyroid antibody titres [53]
ADA/ISPAD (via Kochummen et al., 2018)	TFTs, thyroid antibodies [6]	Soon after T1DM diagnosis [6]	TFT every 1–2 years [6]	Not specified [6]
NICE guidelines (via Mallya et al., 2021)	TFTs [16]	At diagnosis [16]	Annually [16]	Not specified [16]

Source	Recommended Tests	Timing	Frequency	High-Risk Groups
Hansen et al., 2015 (review)	Anti-TPO, anti-TG, TSH [10]	Early onset (8–14 years) [10]	Every 2 years [10]	Families with clustering of T1D or PAS [10]

There is broad consensus that thyroid autoantibody testing and TSH measurement should be performed at T1DM diagnosis [1, 2, 4, 6, 11, 13, 53]. The debate centers on the optimal frequency of subsequent screening and whether to risk-stratify. The ISPAD guidelines recommend repeat screening every 2 years [1, 11], while the ADA suggests every 1–2 years [11], and NICE guidelines recommend annual thyroid function testing [16, 68]. Carreras et al. proposed a differentiated strategy: annual TSH for antibody-positive individuals and biennial screening from puberty through adulthood for initially antibody-negative youth diagnosed before 18 [11].

Mallya et al. raised the important point that thyroid function testing at diagnosis may yield misleading results due to sick euthyroid syndrome, suggesting that only TPO antibody testing (rather than full thyroid function) may be appropriate at initial presentation, with interval thyroid function testing reserved for those with positive antibodies [16].

Impact on Diabetes Management

The clinical consequences of thyroid autoimmunity and dysfunction on diabetes management were addressed by several studies, though comprehensive data were limited.

Hypothyroidism in T1DM patients can decrease insulin requirements and increase the risk of hypoglycemia [4, 8, 10, 39, 53], while hyperthyroidism may worsen glycemic control, increase insulin requirements, and elevate the risk of diabetic ketoacidosis [4, 10, 39]. Głowińska-Olszewska et al. found that T1DM patients with coexisting Hashimoto's thyroiditis had significantly higher mean HbA1c (8.8% vs. 8.1%, $p = 0.04$), higher BMI, and higher waist circumference compared to T1DM patients without thyroid disease [15]. Sobolewska et al. noted higher daily insulin doses in patients with Hashimoto's compared to isolated T1DM [53]. Hansen et al. emphasized that

hypothyroidism in T1DM children can lead to growth disorders from chronic hypoglycemia and decreased thyroid hormone action [10].

The cardiovascular implications were explored by Głowińska-Olszewska et al., who found higher hsCRP and lower vitamin D in T1DM patients with Hashimoto's thyroiditis, although carotid intima-media thickness was not significantly different from T1DM patients without thyroid disease [15]. Łukawska-Tataczuk et al. demonstrated that young women with T1DM and Hashimoto's had higher carotid intima-media thickness and reduced left ventricular longitudinal strain compared to those with T1DM alone [55], with longer Hashimoto's duration correlating with worse segmental cardiac function [44]. Rogers et al. demonstrated that increasing numbers of concomitant autoimmune diseases in T1DM were associated with higher risks of renal failure, ischemic stroke, and myocardial infarction [61].

Samuelsson et al., in a large Swedish register-based study of over 15,000 pediatric T1D patients, found that while almost 20% developed at least one additional autoimmune disease (with thyroid disease being among the most common), this comorbidity was not associated with worse metabolic control or mortality risk [62]. This finding provides some reassurance, though the cardiovascular markers reported by other studies suggest subclinical effects that may manifest over longer timeframes.

Synthesis

The included studies present a largely consistent picture regarding several key aspects of thyroid autoimmunity in pediatric T1DM, though meaningful heterogeneity in prevalence estimates warrants explanation.

Explaining prevalence heterogeneity. The wide range of thyroid autoantibody prevalence (6.7%–44.8%) across studies reflects genuine between-population differences rather than simple measurement error. Three principal factors account for most of the variation. First, *ethnic background* plays a determinative role: the predominantly African American cohort of Kochummen et al. showed markedly lower prevalence (11%) [6] compared to European and Middle Eastern populations (18–30%) [1–3], consistent with known ethnic variation in autoimmune susceptibility. The Celis-Andrade meta-analysis confirmed geographic variation, with the highest latent

polyautoimmunity rates in Asia (23.29%) and Oceania (21.53%) [31]. Second, *timing of measurement* substantially affects estimates: cross-sectional screening at T1DM diagnosis yields lower prevalence (14.5–18%) [1, 18] than cumulative prevalence after years of follow-up (30–34.5%) [2, 3], because seroconversion continues for years after T1DM onset [2]. Third, *assay methodology and positivity thresholds* varied across studies and time periods, with the Herczeg et al. study noting methodological changes over its 10-year study period [13]. The inclusion of TRAb alongside TPOAb and TGAb in the Turkish study likely contributed to its unusually high 44.8% positivity rate [19].

Predictive value of autoantibodies. The evidence converges on TPO antibody positivity at T1DM diagnosis as a clinically meaningful predictor. Carreras et al. quantified the risk at an 8.1-fold increase (95% CI: 4.79–13.69) for thyroid dysfunction in antibody-positive versus antibody-negative patients [11], and Umpierrez et al. found a 17.91-fold increase (95% CI: 3.89–82.54) [12]. However, the clinical significance of this finding depends on the timeframe considered. In the short term (3–5 years), only 14–28.5% of antibody-positive children develop clinical disease [1, 13], suggesting that immediate intervention is not warranted for all antibody-positive patients. Over decades, however, progression rates reach 84% [11], making thyroid autoantibody status a reliable long-term predictor. Critically, initially antibody-negative patients are not without risk: Carreras et al. showed that thyroid dysfunction also developed in this group, particularly among those diagnosed with T1DM before age 18 [11], justifying continued periodic screening.

The female preponderance. The consistently higher prevalence of thyroid autoimmunity in females across diverse populations [1, 2, 7, 13, 61] parallels the well-established sex difference in autoimmune thyroid disease in the general population. Wang et al.'s twin study showing 69% heritability for TPOA [7] combined with the observation that environmental factors causing T1DM are distinct from those causing thyroid autoimmunity suggests that the shared HLA genetic background, rather than a common environmental trigger, accounts for the T1DM-thyroid autoimmunity co-occurrence. The stronger female preponderance in thyroid autoimmunity compared to T1DM itself (which has a more balanced sex ratio) supports this interpretation.

Screening strategy optimization. The data support a risk-stratified screening approach. Measuring TPO antibodies and TSH at T1DM diagnosis provides prognostic information [1, 11], though Mallya et al.'s observation of frequent transient thyroid function abnormalities at diagnosis—particularly in patients presenting with DKA—argues for caution in interpreting TFTs obtained during acute metabolic derangement [16, 17]. A practical approach would test TPO antibodies at diagnosis and reserve thyroid function testing for clinical stabilization. Antibody-positive patients should undergo annual TSH monitoring given their high long-term risk [11, 12], while antibody-negative patients can be screened less frequently (every 2 years) [4, 11] with the understanding that seroconversion occurs at a meaningful rate [2]. In populations with lower baseline risk (e.g., predominantly African American cohorts) [6], the cost-benefit calculus of frequent screening may differ.

Levothyroxine in euthyroid autoimmune thyroiditis. Two studies addressed whether treating euthyroid T1DM patients with autoimmune thyroiditis could prevent disease progression. The RCT by Karges et al. showed that levothyroxine reduced thyroid volume but did not prevent progression to hypothyroidism (conversion rate 9.3% per year in both groups) [18], while Korzeniowska et al.'s observational study suggested that levothyroxine stabilized the autoimmune process based on decreasing anti-TPO levels [20]. The discrepancy likely reflects differences in study design (RCT vs. observational) and outcome measures (clinical hypothyroidism vs. antibody levels). On balance, current evidence does not support routine levothyroxine for euthyroid antibody-positive patients.

COVID-19 era effects. Two studies examined whether the COVID-19 pandemic altered thyroid autoimmunity patterns. Herczeg et al. found that the increase in thyroid autoimmunity prevalence among Hungarian T1DM children occurred during pre-pandemic years but did not continue during the COVID-19 era [13]. Montgomery et al. reported a decrease in autoimmune thyroiditis frequency from 17.8% to 13.9% ($p = 0.045$) during the pandemic in a US cohort [21]. These findings do not support a direct role for SARS-CoV-2 in promoting thyroid autoimmunity in T1DM patients.

DISCUSSION

Prevalence of Thyroid Autoantibodies: Explaining Heterogeneity

The most striking finding of this review is the wide range of thyroid autoantibody prevalence (6.7% to 44.8%) across included studies (1, 16, 19). This heterogeneity is not merely methodological artifact but reflects genuine between-population differences that carry important clinical implications.

Ethnic and geographic variation plays a determinative role. The predominantly African American cohort studied by Kochummen et al. showed a notably low prevalence of thyroid autoimmunity (11%) and clinical thyroid disease (1.3% Hashimoto's), significantly lower than predominantly Caucasian or Middle Eastern populations (1, 2, 3, 6). This suggests that genetic background modulates autoimmune susceptibility independent of T1DM itself. The meta-analysis by Celis-Andrade et al. confirmed geographic variation, with the highest latent polyautoimmunity rates in Asia (23.29%) and Oceania (21.53%) (31). Clinicians in regions with diverse ethnic populations cannot simply apply prevalence estimates from predominantly Caucasian cohorts.

Timing of measurement substantially affects estimates. Cross-sectional screening at T1DM diagnosis typically yields lower prevalence (14.5–18%) than cumulative prevalence after years of follow-up (30–34.5%) (1, 2, 3, 18). Al-Khawari et al. demonstrated that 17.7% of initially antibody-negative patients seroconverted over 4–9 years, yielding a cumulative prevalence of 34.5% (2). This phenomenon has profound clinical implications: a single screening at diagnosis misses a substantial proportion of patients who eventually develop thyroid autoimmunity.

Assay methodology and positivity thresholds also contribute to variation. Herczeg et al. noted methodological changes over their 10-year study period that affected antibody detection rates (13). The Turkish study by Okten et al., which included TRAb alongside TPOAb and TgAb, reported an unusually high 44.8% positivity rate (19). Most studies, however, focus on TPOAb and TgAb, with TPOAb being the more sensitive and specific marker for Hashimoto's thyroiditis (1, 11, 12).

Clinical Thyroid Disease: Hypothyroidism Predominates

Across all studies, hypothyroidism was overwhelmingly more common than hyperthyroidism. The pooled meta-analysis by Nederstigt et al. found hypothyroidism in 9.8% of T1DM patients versus hyperthyroidism in only 1.3% (5). Hashimoto's thyroiditis was the predominant disease type, with Graves' disease reported only sporadically (4, 10, 14). Subclinical hypothyroidism was more common than overt disease in several studies (2, 4, 13), suggesting that many children with thyroid autoimmunity remain asymptomatic for years, with diagnosis dependent on biochemical screening.

The long-term study by Carreras et al. is particularly instructive. Over a mean 30.6-year follow-up of patients diagnosed with T1DM in childhood, 84% of those who were TPO-Ab-positive at diabetes onset eventually developed thyroid dysfunction, with a median time to dysfunction of 5 years (relative risk 8.1, 95% CI: 4.79–13.69) (11). Umpierrez et al. similarly found that TPO-positive patients were 17.91 times more likely to develop hypothyroidism over 18 years (95% CI: 3.89–82.54) (12). These data establish TPO antibody positivity at T1DM diagnosis as a powerful long-term predictor, but with a crucial caveat: in the short term (3–5 years), only 14–28.5% of antibody-positive children develop clinical disease (1, 13). This means that immediate intervention is not warranted for all antibody-positive patients, but they require sustained surveillance.

The Challenge of Thyroid Function Tests at T1DM Diagnosis

A critical clinical nuance identified in this review is the phenomenon of sick euthyroid syndrome at T1DM diagnosis. Mallya et al. found that 31% of newly diagnosed T1DM children had abnormal thyroid function tests at presentation, yet only one child required levothyroxine within one year (16). Children presenting with diabetic ketoacidosis (DKA) had even higher rates of abnormal tests (44% vs. 24% in non-DKA) (16). Balsamo et al. confirmed that thyroid function at T1DM onset is primarily influenced by metabolic derangement rather than true thyroid autoimmunity, with reduced FT3/FT4 conversion ratios compared to non-diabetic controls (17).

This finding has direct clinical implications: performing full thyroid function tests at the time of acute metabolic decompensation risks over-diagnosing thyroid dysfunction, leading to unnecessary interventions or worry. A more prudent approach, as suggested by Mallya et al., is to

measure TPO antibodies at diagnosis (which are unaffected by acute illness) and defer TSH and FT4 measurement until metabolic stabilization (16).

Risk Factors: Female Sex as the Dominant Predictor

Female sex was the most consistent and strongest risk factor across all populations and study designs. In Dempsey et al., 73% of TPO-positive children were female (1). Herczeg et al. reported a significant female predominance ($p < 0.001$) (13). Al-Khawari et al. found 58.7% of antibody-positive patients were female (2). The DCCT/EDIC longitudinal study reported cumulative hypothyroidism of 24.6% in women versus 11.3% in men by year 18 (42). Rogers et al. found that women with T1DM were 1.9 times more likely to have a concomitant autoimmune disease (61). The twin study by Wang et al. demonstrated higher TPOA positivity rates in females across both UK (30% vs. 16%) and US (42% vs. 5%) cohorts (7).

This female preponderance parallels the well-established sex difference in autoimmune thyroid disease in the general population, suggesting that sex hormones or X-chromosome-related genetic factors modulate autoimmune risk independent of T1DM-specific mechanisms. Importantly, T1DM itself has a more balanced sex ratio, supporting the interpretation that shared genetic susceptibility (HLA), rather than a common environmental trigger, accounts for the co-occurrence (7).

Genetic Susceptibility: Heritability and HLA Associations

Wang et al. estimated the heritability of TPO antibodies at 69% (95% CI: 50–82%) using discordant twin pairs, indicating that genetic factors play a substantial role (7). Importantly, the environmental factors causing T1DM were distinct from those driving thyroid autoimmunity in the twin model, suggesting that the co-occurrence is primarily driven by shared genetic background rather than shared environmental exposures.

Specific HLA haplotypes have been implicated. Barker et al. identified HLA associations with organ-specific autoantibody clusters (9). Hansen et al. noted that DRB1*03-DQA1*0501-DQB1*0201 and DRB1*04-DQA1*0301-DQB1*0302 haplotypes confer susceptibility to both T1DM and autoimmune thyroid disease (10). Krzewska et al. reported that persistence of anti-GAD antibodies was associated with thyroid autoimmunity, suggesting that a more aggressive islet

autoimmune process predicts broader autoimmunity (4). These genetic insights have not yet translated into routine clinical risk prediction, but they may guide targeted screening in high-risk families.

Age and Diabetes Duration

Thyroid autoantibody prevalence increases with age, particularly after puberty (2, 8), and with longer T1DM duration (8, 31). The meta-regression by Nderstigt et al. showed that for every 10-year age increase, hypothyroidism prevalence increased by 4.6% (95% CI: 2.6–6.6) (5). Al-Khawari et al. found that thyroid antibodies presented early within the first 5 years of T1DM onset (63.2% vs. 36.8%, $p < 0.05$) and increased after puberty onset (2). Krzewska et al. reported that antibodies typically appear within 2.5–3 years of T1DM progression (4).

These age and duration effects have practical implications: screening cannot be limited to the peri-diagnosis period. Children diagnosed at very young ages remain at risk for seroconversion as they age, and screening should continue through adolescence and young adulthood, as emphasized by Carreras et al. (11).

Progression from Antibody Positivity to Clinical Disease

The annual conversion rate from euthyroid autoimmune thyroiditis to hypothyroidism was reported at 3–18% per year (2) and 9.3% per year in the RCT by Karges et al. (18). Short-term follow-up studies (3–5 years) showed clinical disease rates of 14–28.5% (1, 13), whereas studies with extended follow-up (10–30 years) showed much higher rates: 50% within 10 years (3) and 84% over 30 years (11).

Crucially, initially antibody-negative patients are not without risk. Carreras et al. demonstrated that thyroid dysfunction also developed in initially antibody-negative patients, particularly among those diagnosed with T1DM before age 18 (11). This justifies continued periodic screening even in antibody-negative individuals, albeit at reduced frequency.

Levothyroxine in Euthyroid Autoimmune Thyroiditis

Two studies addressed the question of whether treating euthyroid T1DM patients with autoimmune thyroiditis could prevent disease progression. The randomized controlled trial by Karges et al. showed that levothyroxine reduced thyroid volume but did not prevent progression to

hypothyroidism, with a conversion rate of 9.3% per year in both treated and untreated groups (18). In contrast, the observational study by Korzeniowska et al. suggested that levothyroxine stabilized the autoimmune process based on decreasing anti-TPO levels over 24 months (20). The discrepancy likely reflects differences in study design (RCT vs. observational) and outcome measures (clinical hypothyroidism vs. antibody levels). On balance, current evidence does not support routine levothyroxine for euthyroid antibody-positive patients, although it may be considered in those with goiter or rapid antibody titer increase.

Impact on Diabetes Management and Cardiovascular Risk

Hypothyroidism in T1DM patients can decrease insulin requirements and increase hypoglycemia risk, while hyperthyroidism may worsen glycemic control, increase insulin requirements, and elevate DKA risk (4, 8, 10, 39, 53). Głowińska-Olszewska et al. found that T1DM patients with coexisting Hashimoto's thyroiditis had significantly higher mean HbA1c (8.8% vs. 8.1%, $p = 0.04$), higher BMI, and higher waist circumference (15). Sobolewska et al. noted higher daily insulin doses in Hashimoto's patients (53).

The cardiovascular implications are concerning. Głowińska-Olszewska et al. found higher hsCRP and lower vitamin D in T1DM patients with Hashimoto's (15). Łukawska-Tataczuk et al. demonstrated that young women with T1DM and Hashimoto's had higher carotid intima-media thickness and reduced left ventricular longitudinal strain (44, 55). Rogers et al. showed that increasing numbers of concomitant autoimmune diseases in T1DM were associated with higher risks of renal failure, ischemic stroke, and myocardial infarction (61).

However, a large Swedish register-based study by Samuelsson et al. of over 15,000 pediatric T1D patients found that while almost 20% developed at least one additional autoimmune disease (thyroid disease most common), this comorbidity was not associated with worse metabolic control or mortality risk (62). This finding provides some reassurance, though the subclinical cardiovascular effects reported by others suggest that long-term follow-up is warranted.

COVID-19 Era Effects

Two studies examined whether the COVID-19 pandemic altered thyroid autoimmunity patterns. Herczeg et al. found that the increase in thyroid autoimmunity prevalence among

Hungarian T1DM children occurred during pre-pandemic years but did not continue during the COVID-19 era (13). Montgomery et al. reported a decrease in autoimmune thyroiditis frequency from 17.8% to 13.9% ($p = 0.045$) during the pandemic in a US cohort (21). These findings do not support a direct role for SARS-CoV-2 in promoting thyroid autoimmunity in T1DM patients, contrary to some initial hypotheses.

Screening Recommendations: Toward Risk Stratification

There is broad consensus that thyroid autoantibody testing (at least TPOAb) and TSH measurement should be performed at or soon after T1DM diagnosis (1, 2, 4, 6, 11, 13, 53). The debate centers on optimal frequency of subsequent screening. ISPAD guidelines recommend repeat screening every 2 years (1, 11), ADA suggests every 1–2 years (11), and NICE recommends annual thyroid function testing (16, 68).

Based on the synthesized evidence, a risk-stratified approach is proposed:

- **At diagnosis:** Measure TPO antibodies. Defer TSH/FT4 until metabolic stabilization (at least 2–4 weeks after insulin initiation) to avoid sick euthyroid syndrome confounding (16, 17).
- **If TPO antibody-positive:** Annual TSH monitoring indefinitely, given high long-term risk (84% over 30 years) (11, 12).
- **If TPO antibody-negative:** Screen every 2 years, starting from puberty through adulthood, because seroconversion occurs at meaningful rates (17.7% over 4–9 years) (2, 11).
- **High-risk subgroups requiring more frequent screening:** Females, patients with family history of autoimmune thyroid disease, those with other autoimmune conditions (celiac, Addison's), and patients with specific HLA haplotypes (DR3-DQ2, DR4-DQ8) (4, 7, 9, 10, 28, 76).
- **Ethnic considerations:** In predominantly African American populations with lower baseline prevalence (6), a less intensive screening schedule (e.g., every 2–3 years if antibody-negative) may be cost-effective, though prospective studies are needed.

Research Gaps and Future Directions

Several important gaps remain. First, cost-effectiveness studies of different screening frequencies in pediatric T1DM are lacking, particularly for non-Caucasian populations. Second, the optimal age to discontinue screening (if ever) is unknown. Third, the role of newer biomarkers (e.g., type I interferon activity, Th1 chemokines) in predicting progression remains investigational (56, 63). Fourth, the impact of early detection and treatment of subclinical hypothyroidism on cardiovascular outcomes and quality of life in children has not been rigorously studied. Fifth, the interaction between thyroid autoimmunity and other T1DM comorbidities (celiac disease, autoimmune gastritis) requires further exploration (38, 40, 41, 51, 60, 64, 69).

CONCLUSION AND RECOMMENDATIONS

Summary of Key Findings

This systematic review of 80 sources demonstrates that thyroid autoimmunity affects approximately 15–30% of children with type 1 diabetes mellitus, with hypothyroidism (pooled prevalence 9.8%) being far more common than hyperthyroidism (1.3%). Female sex is the strongest risk factor, with females 1.9–2.4 times more likely to develop thyroid autoimmunity. Heritability of TPO antibodies is estimated at 69%, and specific HLA haplotypes (DR3-DQ2, DR4-DQ8) confer susceptibility to both conditions.

TPO antibody positivity at T1DM diagnosis is a powerful long-term predictor: 84% of positive patients develop thyroid dysfunction over 30 years (median time 5 years). However, short-term progression rates are lower (14–28.5% over 3–5 years), and initially antibody-negative patients remain at risk for seroconversion (17.7% over 4–9 years). Thyroid function tests at T1DM diagnosis are frequently abnormal due to sick euthyroid syndrome, particularly during DKA, and should be deferred until metabolic stabilization.

Levothyroxine therapy in euthyroid antibody-positive patients reduces thyroid volume but does not prevent progression to hypothyroidism and is not routinely recommended. Coexisting thyroid autoimmunity may worsen glycemic control, increase insulin requirements, and elevate cardiovascular risk markers, though large registry studies have not shown increased mortality.

Recommendations for Clinical Practice

1. **All children at T1DM diagnosis:** Measure TPO antibodies. Defer TSH and FT4 for at least 2–4 weeks after insulin initiation and metabolic stabilization.
2. **If TPO antibody-positive:** Annual TSH monitoring indefinitely.
3. **If TPO antibody-negative:** TSH screening every 2 years, starting from puberty (approximately age 10–12 years) and continuing through young adulthood (at least age 30).
4. **High-risk groups (females, family history, other autoimmune diseases, specific HLA haplotypes):** Consider more frequent screening (annual even if antibody-negative).
5. **Do not start levothyroxine** in euthyroid antibody-positive children without biochemical hypothyroidism or goiter.
6. **In predominantly African American populations,** a lower index of suspicion and less frequent screening may be appropriate, though individual clinical judgment remains essential.

Suggestions for Future Research

1. Cost-effectiveness analyses of annual vs. biennial screening in diverse ethnic pediatric T1DM populations.
2. Prospective studies to determine the optimal age to discontinue screening.
3. Randomized controlled trials of early levothyroxine intervention in subclinical hypothyroidism on long-term cardiovascular and neurocognitive outcomes.
4. Validation of novel biomarkers (type I interferon, Th1 chemokines) for predicting rapid progression to clinical disease.
5. Large, multi-ethnic cohort studies to refine risk stratification algorithms that incorporate genetic, demographic, and autoantibody data.

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