

Clinical and Laboratory Assessment of Thyroid Function in Patients with Suspected Endocrine Disorders: An Illustrative Analysis

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Abstract

Background: Suspected thyroid dysfunction commonly presents with nonspecific complaints, making biochemical confirmation essential. This illustrative study examined agreement between clinical suspicion and laboratory classification while demonstrating a practical outpatient assessment pathway.

Objective: To describe thyroid-function patterns and evaluate the contribution of symptoms, thyroid autoantibodies, and repeat testing in a simulated endocrine-referral population.

Methods: A synthetic dataset represented 180 adults undergoing assessment for suspected endocrine disorders. Clinical evaluation included symptom history, pulse measurement, and thyroid examination. Serum thyroid-stimulating hormone and free thyroxine were assessed in all patients; free triiodothyronine was assessed when thyroid-stimulating hormone was suppressed. Thyroid peroxidase antibodies were evaluated in hypothyroid biochemical categories. Descriptive comparisons were prespecified. No actual patient records or biological specimens were used.

Results: Normal biochemical thyroid function occurred in 114 patients (63.3%). Overt hypothyroidism affected 18 (10.0%), subclinical hypothyroidism 24 (13.3%), overt hyperthyroidism 12 (6.7%), and subclinical hyperthyroidism 12 (6.7%). Thyroid peroxidase antibodies were positive in 29 of 42 hypothyroid-pattern cases (69.0%). Fatigue occurred in 44 of 66 patients with biochemical dysfunction and 50 of 114 with normal results. Eight initially subclinical hypothyroid profiles normalized on repeat testing.

Conclusion: These simulated observations illustrate why symptoms alone cannot establish thyroid dysfunction. Sequential biochemical assessment, selective antibody testing, and confirmation of mild abnormalities support cautious classification. The numerical findings are educational examples, not clinical evidence.

Keywords: thyroid function, thyroid-stimulating hormone, hypothyroidism, hyperthyroidism, thyroid autoantibodies, laboratory assessment, simulated data

1. Introduction

Thyroid dysfunction is an important consideration in the evaluation of patients with suspected endocrine disorders because thyroid hormones influence metabolism, thermoregulation,

cardiovascular function, and neuropsychological well-being. Both hormone deficiency and excess can produce clinically significant disturbances, yet their manifestations often overlap with those of other endocrine conditions and common non-endocrine illnesses. Fatigue, weight change, palpitations, altered bowel habits, menstrual irregularities, and impaired concentration may prompt thyroid assessment, but none of these findings alone reliably establishes a diagnosis. Consequently, evaluating thyroid function requires integration of clinical observations with appropriately interpreted laboratory measurements.

The clinical assessment provides essential context for selecting tests and interpreting their results. Symptom duration, medication exposure, previous thyroid disease, family history, pregnancy status, and coexisting illness may influence the likelihood of thyroid dysfunction or alter measured hormone concentrations. Physical examination may identify goiter, nodules, tremor, changes in heart rate, or features suggestive of hypothyroidism, although findings can be subtle or absent, particularly in mild disease. In patients referred for suspected endocrine disorders, the diagnostic challenge is amplified by heterogeneous presentations and the possibility that symptoms arise from more than one underlying condition.

Serum thyroid-stimulating hormone is commonly used as an initial biochemical test when primary thyroid dysfunction is suspected. Free thyroxine measurement helps distinguish overt from subclinical abnormalities and is particularly important when pituitary or hypothalamic disease is a concern. Measurement of triiodothyronine may provide additional information in selected patients with suspected thyrotoxicosis, while thyroid autoantibodies can support assessment of an autoimmune etiology when clinically indicated. Nevertheless, laboratory findings are not independent of clinical circumstances. Acute illness, certain medications, assay interference, and physiological variation can complicate interpretation, and a single abnormal result may not establish persistent thyroid disease.

Discordance between clinical presentation and biochemical findings is therefore a relevant focus of thyroid evaluation. Patients with prominent symptoms may have results within laboratory reference intervals, whereas biochemical abnormalities may be detected in individuals with few recognizable signs. Subclinical patterns require particular caution because their clinical significance varies with the degree and persistence of the abnormality and the patient's broader risk profile. Describing these patterns in a clinically defined population may clarify the diagnostic contribution and limitations of routine assessment without assuming that every biochemical deviation explains the presenting complaint.

The present study aimed to assess clinical features and laboratory indicators of thyroid function in patients presenting with suspected endocrine disorders. Specifically, it sought to characterize thyroid functional patterns using prespecified biochemical criteria and examine their relationship with reported symptoms and physical findings. By considering clinical and laboratory information together, the study was intended to describe the spectrum of thyroid-related abnormalities in this population and assess the extent of agreement between clinical suspicion and biochemical classification. Such findings may inform a more contextual approach to evaluating patients whose presentations raise concern for thyroid dysfunction.

2. Materials and Methods

A prospective, cross-sectional observational study was designed to evaluate clinical findings and biochemical thyroid status among adults referred for suspected endocrine disorders. Recruitment was planned over 12 consecutive months at a tertiary outpatient endocrinology service. Eligible participants would be aged 18 years or older and referred because of symptoms, examination findings, or preliminary laboratory abnormalities suggesting endocrine dysfunction. Consecutive recruitment would reduce discretionary selection. The protocol required institutional ethics committee approval before recruitment, written informed consent, and de-identification of research records. Clinically important abnormalities would be communicated to the treating physician without delaying necessary care.

Exclusion criteria comprised pregnancy, the first postpartum year, acute systemic illness requiring hospitalization, thyroid surgery or radioiodine treatment, and current thyroid hormone replacement or antithyroid therapy. These conditions require different interpretive frameworks or directly alter

thyroid function. Patients receiving amiodarone, lithium, or systemic glucocorticoids would also be excluded. Other medications and supplements, including biotin, would be documented. Participants using high-dose biotin would undergo sampling only after an interruption consistent with laboratory guidance and clinical safety. Suspected pituitary disease would not constitute an exclusion, allowing assessment of potentially discordant thyroid profiles.

A recruitment target of 240 participants was selected. Assuming a thyroid dysfunction prevalence of 20%, approximately 246 participants would provide an absolute precision of five percentage points around a prevalence estimate at a 95% confidence level. The operational target therefore offered similar precision while remaining feasible within the recruitment period. Because the true prevalence in this referral population was uncertain, precision would be reported using the observed confidence interval rather than inferred from the planning assumption.

A trained clinician would collect information using a standardized case report form before reviewing study laboratory results. Recorded variables would include age, sex, referral indication, symptom duration, comorbidities, medication exposure, smoking, and family history of thyroid disease. Symptoms assessed would include fatigue, weight change, heat or cold intolerance, altered bowel habits, palpitations, menstrual disturbance, and neck swelling. Examination would document body mass index, pulse, blood pressure, tremor, skin changes, reflexes, thyroid enlargement, palpable nodules, and eye signs. Individual findings would be analyzed rather than combined into an unvalidated diagnostic score.

Venous blood would be collected between 08:00 and 10:00. Serum would be separated within two hours and analyzed according to laboratory procedures. Thyroid-stimulating hormone (TSH) and free thyroxine (FT4) would be measured in all participants using a single automated immunoassay platform. Free triiodothyronine would be measured when TSH was suppressed, and thyroid peroxidase antibodies when elevated TSH or clinical features suggested autoimmune thyroid disease. Manufacturer-specified, locally verified adult reference intervals would guide interpretation. Internal controls at two concentration levels and participation in external quality assessment would support analytical reliability. Laboratory personnel would be unaware of the structured clinical assessment.

Primary hypothyroidism would be classified as elevated TSH with reduced FT4, and subclinical hypothyroidism as elevated TSH with normal FT4. Overt hyperthyroidism would require suppressed TSH with elevated FT4 or free triiodothyronine; subclinical hyperthyroidism would require suppressed TSH with both hormones within reference intervals. Reduced FT4 with low or inappropriately normal TSH would prompt evaluation for central hypothyroidism rather than automatic classification. Borderline or discordant results would undergo clinical review and repeat testing after six to eight weeks when appropriate; initial abnormalities would not automatically imply persistent disease.

Analyses would summarize continuous variables using means and standard deviations or medians and interquartile ranges, and categorical variables using counts and percentages. The primary outcome would be the proportion with biochemical thyroid dysfunction at presentation, with 95% confidence intervals. Exploratory logistic regression would assess associations with prespecified clinical variables, limiting model complexity according to outcome frequency. Missing data would be reported explicitly. Findings would be interpreted as associations within a referral population, not causal relationships or community prevalence estimates.

3. Results

The following results describe an illustrative dataset rather than observed patient data. The analysis included 300 adults evaluated for suspected endocrine disorders, comprising 222 women (74.0%) and 78 men (26.0%). Median age was 42 years (interquartile range [IQR], 32–55), and 84 participants (28.0%) were aged 55 years or older. Common reasons for referral included persistent fatigue, unexplained weight change, palpitations, menstrual irregularity, and suspected thyroid enlargement. Multiple presenting complaints were frequently recorded. Patients receiving thyroid hormone replacement or antithyroid treatment, pregnant patients, and those with acute severe illness were not included in this illustrative cohort.

Using laboratory reference intervals of 0.4–4.0 mIU/L for thyroid-stimulating hormone (TSH) and

12–22 pmol/L for free thyroxine (FT4), 180 patients (60.0%) had biochemical euthyroidism and 120 (40.0%) had an abnormal thyroid profile. Subclinical hypothyroidism was the most frequent abnormality, identified in 48 patients (16.0%), followed by overt primary hypothyroidism in 30 (10.0%), subclinical hyperthyroidism in 24 (8.0%), and overt hyperthyroidism in 18 (6.0%). Subclinical categories required normal circulating free thyroid hormone concentrations, whereas overt categories required corresponding hormone abnormalities. Thyroid dysfunction was identified in 94 women (42.3% of women) and 26 men (33.3% of men). These proportions describe the referred population and were not interpreted as population prevalence estimates.

Median TSH was 2.1 mIU/L (IQR, 1.4–2.9) in euthyroid patients, 6.8 mIU/L (IQR, 5.2–8.9) in those with subclinical hypothyroidism, and 22.4 mIU/L (IQR, 14.6–38.2) in those with overt hypothyroidism. Corresponding median FT4 concentrations were 16.2 pmol/L (IQR, 14.5–18.1), 14.1 pmol/L (IQR, 12.9–15.6), and 8.3 pmol/L (IQR, 6.4–10.2), respectively. Median TSH was 0.18 mIU/L (IQR, 0.09–0.28) in subclinical hyperthyroidism and 0.02 mIU/L (IQR, 0.01–0.04) in overt hyperthyroidism. Median FT4 in these groups was 18.3 pmol/L (IQR, 16.5–20.1) and 31.6 pmol/L (IQR, 26.8–39.4), respectively. No patient had a low FT4 concentration with an inappropriately normal or low TSH in this dataset.

Clinical manifestations overlapped substantially between biochemical groups. Fatigue was reported by 58 of 78 patients with hypothyroid profiles (74.4%), compared with 90 of 180 euthyroid patients (50.0%). Weight gain occurred in 39 patients with hypothyroid profiles (50.0%) and 54 euthyroid patients (30.0%), while cold intolerance was recorded in 31 (39.7%) and 27 (15.0%), respectively. Among the 42 patients with hyperthyroid profiles, palpitations occurred in 26 (61.9%), heat intolerance in 21 (50.0%), and unintentional weight loss in 18 (42.9%). The corresponding frequencies among euthyroid patients were 36 (20.0%), 22 (12.2%), and 18 (10.0%). No individual complaint was confined to a single biochemical category.

Physical findings were more prominent in overt than subclinical dysfunction, although they were not uniformly present. Bradycardia, defined as a resting heart rate below 60 beats/minute, was documented in 9 of 30 patients with overt hypothyroidism (30.0%), compared with 5 of 48 with subclinical hypothyroidism (10.4%). Tachycardia, defined as a resting heart rate above 100 beats/minute, occurred in 10 of 18 patients with overt hyperthyroidism (55.6%) and 4 of 24 with subclinical hyperthyroidism (16.7%). Palpable thyroid enlargement was present in 45 patients overall (15.0%), including 21 euthyroid patients. Thus, enlargement did not consistently correspond to biochemical dysfunction.

Thyroid peroxidase antibodies were measured in all participants and were positive in 66 (22.0%), according to the assay-specific threshold. Positivity was observed in 24 of 30 patients with overt hypothyroidism (80.0%), 30 of 48 with subclinical hypothyroidism (62.5%), and 8 of 180 euthyroid patients (4.4%). Two patients in each hyperthyroid category were antibody-positive. Overall, 54 of 78 patients with hypothyroid profiles (69.2%) had detectable antibody concentrations above the threshold. Antibody positivity supported an autoimmune contribution in these patients but did not independently establish the cause of every abnormal profile.

Across the cohort, subclinical abnormalities accounted for 72 of 120 abnormal profiles (60.0%). Symptoms commonly associated with thyroid disease were also frequent among biochemically euthyroid participants, while some patients with abnormal laboratory findings had few characteristic manifestations. The observed clinical–biochemical overlap limited discrimination based on symptoms or examination alone. Because classification was based on a single assessment, these findings did not establish persistence, progression, or spontaneous resolution of thyroid dysfunction. No conclusions regarding treatment response or subsequent clinical outcomes were drawn from this cross-sectional dataset.

4. Discussion

The clinical and laboratory assessment of thyroid function in patients with suspected endocrine disorders highlights the importance of interpreting biochemical findings within the broader clinical context. Symptoms commonly attributed to thyroid dysfunction, including fatigue, weight change, palpitations, and altered bowel habits, are frequent reasons for endocrine evaluation but have limited diagnostic specificity. The central implication of this assessment is therefore not that any individual

symptom reliably identifies thyroid disease, but that a structured combination of history, examination, and appropriately selected laboratory tests provides a more defensible basis for diagnosis. This distinction is particularly relevant in referral populations, where overlapping endocrine and nonendocrine conditions may influence both presentation and test interpretation.

Clinical features remain valuable for establishing pretest probability and determining the urgency of investigation. Combinations such as persistent tachycardia, tremor, heat intolerance, and unintentional weight loss increase suspicion of thyrotoxicosis, whereas cold intolerance, constipation, dry skin, and slowing of activity may suggest hypothyroidism. Nevertheless, neither symptom cluster is sufficiently sensitive or specific to substitute for biochemical confirmation. Older adults may have less typical manifestations, and symptoms can also be modified by medication use, comorbidity, and disease duration. Conversely, patients with mild biochemical abnormalities may report few complaints. Clinical assessment should consequently guide testing without becoming a basis for attributing all nonspecific symptoms to thyroid dysfunction.

Serum thyroid-stimulating hormone is generally the most informative initial investigation when primary thyroid dysfunction is suspected and hypothalamic-pituitary function is intact. Its interpretation alongside free thyroxine helps distinguish overt dysfunction from subclinical biochemical patterns. An elevated thyroid-stimulating hormone concentration with reduced free thyroxine supports primary hypothyroidism, whereas suppressed thyroid-stimulating hormone with elevated free thyroxine and/or triiodothyronine supports overt thyrotoxicosis. These patterns identify functional states rather than necessarily establishing their cause. Thyrotoxicosis, for example, may reflect increased hormone synthesis, destructive thyroiditis, or exogenous hormone exposure. Maintaining this distinction is important because treatment depends on the underlying mechanism, not simply the direction of laboratory abnormality.

Subclinical thyroid dysfunction requires especially cautious interpretation. An abnormal thyroid-stimulating hormone concentration with free thyroid hormones within the reference range may represent persistent early disease, but it can also be transient. A single measurement is therefore insufficient to establish persistence in many clinically stable patients. Repeat testing after an appropriate interval, informed by the degree of abnormality and clinical circumstances, can reduce premature labeling and unnecessary treatment. Decisions about intervention should also consider age, symptoms, pregnancy status or reproductive plans, cardiovascular disease, skeletal risk, and evidence of thyroid autoimmunity. Mild biochemical deviations should not automatically be assumed to explain substantial symptom burden, particularly when alternative causes remain plausible.

Discordance between clinical presentation and laboratory results warrants reassessment rather than immediate therapeutic escalation. Acute systemic illness, recovery from illness, and certain medications can alter thyroid function tests without indicating intrinsic thyroid disease. Glucocorticoids and dopamine-related therapies may suppress thyroid-stimulating hormone, while amiodarone can produce complex changes in thyroid hormone metabolism as well as genuine dysfunction. Supplement use is also relevant because biotin can interfere with some immunoassays and generate misleading results. When the biochemical pattern is unexpected, reviewing exposures, confirming sampling circumstances, and discussing potential assay interference with the laboratory may be more informative than simply expanding the investigation panel.

A further consideration is that a normal or modestly abnormal thyroid-stimulating hormone concentration does not exclude central hypothyroidism. In patients with pituitary symptoms, known hypothalamic-pituitary disease, or evidence of multiple hormone deficiencies, free thyroxine must be interpreted independently of the usual thyroid-stimulating hormone screening logic. Low free thyroxine with an inappropriately normal or low thyroid-stimulating hormone concentration should prompt consideration of central disease, while recognizing that severe illness and analytical factors can produce similar findings. This issue has particular relevance in a population evaluated for suspected endocrine disorders rather than isolated thyroid complaints. Where pituitary dysfunction is suspected, assessment of adrenal function is important before initiating thyroid hormone replacement.

Additional investigations should be selected to answer specific clinical questions. Thyroid peroxidase

antibodies may support an autoimmune basis for hypothyroidism and help contextualize the likelihood of progression in persistent subclinical disease. Thyroid-stimulating hormone receptor antibodies can assist in identifying Graves disease when the cause of thyrotoxicosis is uncertain. Antibody positivity alone, however, does not establish current functional impairment or justify treatment. Similarly, ultrasonography evaluates thyroid structure rather than hormone production and should not be used routinely to explain nonspecific symptoms or isolated biochemical abnormalities. Its role is clearer when examination identifies a nodule, asymmetric enlargement, or another structural concern.

The interpretation of this type of clinical assessment is constrained by referral selection and the timing of testing. Patients presenting with suspected endocrine disease are not representative of the general population, limiting extrapolation of disease frequencies or symptom profiles. Cross-sectional measurements cannot reliably distinguish transient abnormalities from persistent dysfunction or determine whether thyroid abnormalities preceded reported symptoms. Symptom reporting may also be influenced by recall, concurrent illness, and prior knowledge of thyroid disease. Laboratory reference intervals, assay characteristics, medication exposure, and incomplete characterization of comorbidities introduce additional uncertainty. These considerations argue against causal conclusions based solely on associations between symptoms and biochemical categories.

Overall, thyroid evaluation is best approached as an iterative clinical process rather than a single diagnostic threshold. Initial biochemical classification should be followed, where appropriate, by confirmation, etiological assessment, and individualized consideration of treatment. Future prospective work would benefit from standardized symptom assessment, repeat laboratory measurements, explicit documentation of interfering exposures, and follow-up of patient-centered outcomes. Such data could help determine which combinations of clinical and biochemical findings predict persistent disease and meaningful benefit from intervention.

5. Conclusion

This study underscores the complementary value of clinical evaluation and laboratory testing in assessing thyroid function among patients presenting with suspected endocrine disorders. Symptoms and physical findings can guide the initial diagnostic assessment, but their nonspecific nature limits their ability to distinguish thyroid dysfunction from other endocrine and nonendocrine conditions. Interpretation of thyroid function tests should therefore remain anchored in the clinical presentation rather than relying on either biochemical results or symptoms in isolation.

Serum thyroid-stimulating hormone, interpreted alongside free thyroxine when indicated, provides a practical framework for identifying patterns compatible with primary hypothyroidism and hyperthyroidism. However, apparently discordant results require careful reassessment, particularly in patients with intercurrent illness, relevant medication exposure, possible assay interference, or suspected hypothalamic–pituitary disease. Mild biochemical abnormalities should not automatically be considered persistent thyroid disease. Where clinically appropriate, repeat testing and review of potentially reversible influences may reduce diagnostic misclassification and unnecessary treatment.

The findings support a targeted approach in which additional investigations, including thyroid autoantibodies or imaging, are selected according to the biochemical pattern and specific clinical indications. Laboratory reference intervals, age, pregnancy status, and the broader clinical context remain important considerations when interpreting results. Biochemical classification alone does not establish the cause of an abnormality or determine whether treatment will provide meaningful benefit.

Interpretation of this study should account for the selected population of patients already suspected of having endocrine disease, which limits extrapolation to asymptomatic community populations. Furthermore, clinical and biochemical assessment at presentation cannot, by itself, establish persistence, progression, or treatment responsiveness. Prospective studies incorporating repeat measurements and patient-centered outcomes are needed to clarify these issues. Overall, an integrated, context-sensitive assessment offers a defensible basis for identifying clinically relevant thyroid dysfunction while avoiding overinterpretation of isolated abnormalities and supporting appropriate follow-up, further investigation, and individualized management.

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