Saudi Journal of Medicine and Public Health

https://saudijmph.com/index.php/pub

https://doi.org/10.64483/jmph-114

Interpreting Thyroid Function Tests in Difficult Clinical Contexts: A Practical Approach to Avoiding Diagnostic Pitfalls and Accurately Diagnosing Thyroid Dysfunction

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Abstract

Background: Thyroid function tests (TFTs) are essential for diagnosing thyroid disease, but their interpretation is problematic during pregnancy, critical illness, and biotin interference due to physiological changes and analytic interference. **Aim:** To provide a practical manual for clinicians to circumvent diagnostic pitfalls and correctly interpret TFTs in these scenarios. **Methods:** A narrative review (PubMed, Scopus, Web of Science; 2000–2025) of English peer-reviewed studies on TFT interpretation in pregnancy, non-thyroidal illness syndrome (NTIS), and biotin interference. Data were summarized to highlight physiological processes, diagnostic challenges, and management strategies. **Results:** Pregnancy requires trimester-specific TFT ranges because of hormonal change, NTIS needs distinction between adaptive responses and true hypothyroidism, and biotin interference needs assay awareness and supplement withdrawal. Trimester-specific ranges, conservative NTIS management, and non-biotin-based assays improve diagnostic accuracy. **Conclusion:** Understanding of physiological and analytical aspects, use of good-quality assays, and adherence to guidelines are crucial for the accurate interpretation of TFT, which results in improved patient outcomes in difficult clinical circumstances.

Keywords: Thyroid function tests, pregnancy, non-thyroidal illness syndrome, biotin interference, diagnostic accuracy.

1. Introduction

Thyroid function tests (TFTs), comprising thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3), are key diagnostic tests for evaluating thyroid function and diagnosing thyroid gland disorders such as hypothyroidism and hyperthyroidism (Garber et al., 2012). They provide quantitative measurements of thyroid hormone levels and pituitary feedback, enabling clinicians to establish thyroid status. However, TFT interpretation is challenging in complex clinical contexts—pregnancy, severe illness, and biotin interference—in which physiological processes or analytical errors obscure true thyroid function, with potential for misdiagnosis and inappropriate treatment (Krassas et al., 2010).

In pregnancy, thyroid physiology is significantly changed by increased estrogen, hCG, and TBG, which alter TFT profiles and necessitate trimester-specific reference ranges to prevent misdiagnosis of thyroid dysfunction (Glinoer, 1997). For instance, hCG's thyroid-stimulating activity may suppress TSH, mimicking hyperthyroidism, and elevated TBG concentrates total thyroid hormone levels without necessarily affecting free hormone levels (Laurberg et al., 2011). Misinterpretation of the changes can lead to unjustified interventions or disregard of true thyroid disease, both of which are associated with adverse maternal and fetal outcomes, including miscarriage, preterm delivery, and impaired neurodevelopment (Kwakkel et al., 2011).

Critical illness typically induces non-thyroidal illness syndrome (NTIS), low FT3, variable FT4, and normal or low TSH, which is an adaptive reaction to systemic stress rather than intrinsic thyroid disease (Van den Berghe, 2014). NTIS is frequent in sepsis, trauma, and organ failure, and its TFT profile can resemble hypothyroidism, leading to a diagnostic challenge (Fliers et al., 2015). Thyroid hormone replacement treatment in NTIS is not indicated, as this may exacerbate catabolism, although it is necessary to distinguish NTIS from true hypothyroidism, particularly in individuals with underlying thyroid illness (Warner & Beckett, 2010).

Interference due to biotin is an increasing issue and is secondary to the widespread use of high-dose biotin supplements for either cosmetic or therapeutic purposes (Elston et al., 2016). Biotin

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Receive Date: 10 November 2024, Revise Date: 30 November 2024, Accept Date: 31 December 2024

interferes with biotin-dependent immunoassays, which are prevalent in TFTs, to cause spuriously high FT4 and FT3 or spuriously low TSH, mimicking hyperthyroidism (Wijeratne et al., 2012; Fathi-Karkan et al., 2024). The growing prevalence of biotin intake, at doses up to 10 mg in over-the-counter supplements, makes it important for clinicians to be cognizant and take measures to prevent this analytical pitfall (Li et al., 2017).

This review combines evidence from peer-reviewed publications, from clinical guidelines through to observational studies and experimental studies, to provide a comprehensive and practical guide for the clinician. It covers the physiological and analytical pitfalls of TFT interpretation in pregnancy, critical illness, and biotin interference and provides evidence-based strategies for preventing diagnostic pitfalls.

Methods

This narrative review was conducted by a systematic search of PubMed, Scopus, and Web of Science for articles published between January 2000 and October 2025. The search was conducted using a combination of MeSH terms and keywords, including "thyroid function tests," "thyroid-stimulating hormone," "free thyroxine," "free triiodothyronine," "pregnancy," "critical illness," "non-thyroidal illness syndrome," "biotin interference," and "thyroid dysfunction." Boolean operators (AND, OR) were used to restrict the search, offering wide coverage of the literature.

Inclusion was restricted to peer-reviewed articles in the English language that explicitly addressed the interpretation of TFTs in the context of pregnancy, critical illness, or biotin interference. Articles were included if they provided data on physiological mechanisms, diagnostic pitfalls, clinical outcomes, or management. Non-peer-reviewed articles, case reports with low generalizability, and studies not applicable to the specified clinical contexts were excluded. 40 papers were selected, such as clinical guidelines (e.g., American Thyroid Association guidelines), prospective and retrospective observational studies, and experimental studies on assay methods and thyroid physiology.

Data were extracted on the following principal themes: physiological changes that affect TFTs, diagnostic pitfalls, and evidence-based practice recommendations for accurate interpretation. Data were synthesized narratively to create a cogent overview of each clinical scenario, with a focus on pragmatic relevance to clinicians. Two tables were constructed to summarize key information: one of trimester-specific TFT reference ranges during pregnancy, and one of diagnostic considerations and management in NTIS and biotin interference. The review was conducted according to narrative review standards, prioritizing clarity, clinical usefulness, and synthesis of modern evidence to guide practice.

Physiological and Analytical Challenges in TFT Interpretation

Pregnancy

Pregnancy induces profound changes in thyroid physiology secondary to hormonal and metabolic changes that significantly affect TFT results (Glinoer, 1997). These are mediated mainly by three mechanisms: estrogen rise, hCG rise, and rising TBG levels. Estrogen stimulates the hepatic production of TBG, a thyroid hormone binder, which increases total T4 and T3 levels without necessarily altering free hormone levels (Soldin et al., 2004). hCG, which peaks in the first trimester, shares structural homology with TSH and possesses direct thyroid hormone stimulatory action, often suppressing TSH beneath non-pregnant reference ranges (Laurberg et al., 2011). Additionally, increased maternal metabolic demands and placental thyroid hormone metabolism further complicate TFT interpretation (Casey & Leveno, 2006).

This physiological change necessitates trimester-specific reference ranges for TSH, FT4, and FT3 to avoid misdiagnosis (Alexander et al., 2017). For example, a TSH level of 3.5 mIU/L, which is normal in the non-pregnant state, may be indicative of subclinical hypothyroidism during the first trimester, when the upper limit is typically 2.5 mIU/L (Sahib et al., 2024). Conversely, suppressed TSH due to stimulation by hCG can mimic hyperthyroidism, particularly if FT4 is elevated (Haddow et al., 1999; Hazazi, 2025). Neglect of trimester-specific ranges may lead to misdiagnosis, such as the unjustified commencement of levothyroxine for supposed hypothyroidism or the lack of recognition of true thyroid dysfunction (Maraka et al., 2016).

Maternal thyroid dysfunction is associated with significant adverse outcomes, including miscarriage, preterm delivery, gestational hypertension, and impaired fetal neurodevelopment (Krassas et al., 2010). Overt hypothyroidism, as characterized by elevated TSH and low FT4, requires the prompt initiation of levothyroxine to prevent these risks (De Groot et al., 2012). Subclinical hypothyroidism, as indicated by elevated TSH with normal FT4, is controversial due to a lack of consistency in TSH cutoffs and a lack of sufficient evidence of treatment benefit (Maraka et al., 2016). Universal TSH screening in high-risk pregnant women, i.e., those with autoimmune thyroid disease or history of miscarriage, and targeted levothyroxine therapy for overt hypothyroidism have been recommended by the American Thyroid Association (ATA) (Feldt-Rasmussen & Rasmussen, 2010).

Autoimmune thyroid disease, and Hashimoto's thyroiditis in particular, also bewilders TFT interpretation because anti-thyroid peroxidase (TPO) antibodies are associated with a risk of hypothyroidism and adverse pregnancy outcomes (Krassas et al., 2010). The ATA suggests TPO

antibody status monitoring in pregnant women with borderline TFTs to guide management (Soh & Aw, 2019). Besides, FT4 and FT3 assays can be affected by assay variability in the setting of high TBG levels, rendering the use of valid methods such as liquid chromatography-tandem mass spectrometry (LC-MS/MS) essential for the accurate quantification of free hormones (Surks et al., 2004).

Diagnostic Difficulties in Pregnancy

Pregnancy is beset by physiological changes that can mimic thyroid disease, thus rendering diagnosis extremely difficult. In the first trimester, hCG levels peak at 7 to 11 weeks, stimulating thyroid hormone production and often suppressing TSH to as little as 0.1 mIU/L, replicating hyperthyroidism (Laurberg et al., 2011). This is most pronounced in that subset of individuals with hyperemesis gravidarum, where elevated hCG exacerbates the suppression of TSH and elevation of FT4 (Glinoer, 1997). Conversely, elevated TBG increases total T4 and T3, but FT4 and FT3 are relatively stable, requiring assays that effectively distinguish between free and bound hormones (Soldin et al., 2004).

Failure to use trimester-specific reference ranges can result in a misdiagnosis. For instance, a TSH of 3.5 mIU/L may be normal in the second trimester (upper limit ~3.0 mIU/L) but abnormal in the first trimester (upper limit ~2.5 mIU/L), potentially leading to inappropriate levothyroxine therapy (Alexander et al., 2017; Maraka et al., 2016). Similarly, elevated FT4 in the first trimester may reflect hCG stimulation rather than true hyperthyroidism, necessitating clinical correlation with symptoms and antibody status (Glinoer, 1997). Risk factors for the mother, such as autoimmune thyroid disease or iodine deficiency, also muddy the waters, as they increase the likelihood of actual thyroid dysfunction (Krassas et al., 2010).

To surmount these challenges, the ATA recommends trimester-specific TSH cutoffs (e.g., 0.1–2.5 mIU/L in the first trimester, 0.2–3.0 mIU/L in the second, and 0.3–3.0 mIU/L in the third) and FT4 measurements using high-precision assays like LC-MS/MS (Aljehani & Alhayek, 2024; Soldin et al., 2004). Clinicians also need to assess clinical symptoms, family history, and TPO antibody status to differentiate physiological changes from pathological conditions. For example, suppressed TSH, raised FT4, and positive TPO antibodies in pregnancy may require further investigation for Graves' disease, but TSH suppression alone is generally benign (Krassas et al., 2010; Barbesino, 2016). Monitoring throughout pregnancy is necessary, particularly in individuals with known thyroid disease, to adjust therapy and minimize risks (Alexander et al., 2017). Figure 1 shows how pregnancy-related factors affect thyroid test interpretation.

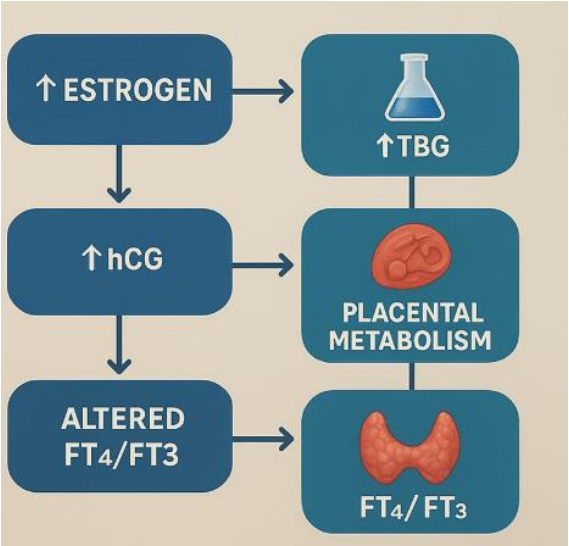

Figure 1. Physiological and Analytical Factors Influencing Thyroid Function Tests in Pregnancy

Critical Illness and Non-Thyroidal Illness Syndrome

Severe illness regularly results in non-thyroidal illness syndrome (NTIS), or euthyroid sick syndrome, with deranged TFT profiles in the absence of intrinsic thyroid illness (Fliers et al., 2015). NTIS is prevalent in the intensive care unit, where it is found in sepsis patients, trauma, burns, or organ failure, and occurs in up to 70% of critically ill patients (Van den Berghe, 2014). The typical TFT pattern is low FT3, normal or low FT4, and normal or low TSH, an adaptive response to reduce metabolic demand in the context of systemic stress (Vassiliadi et al., 2021).

The pathophysiology of NTIS is complex. Cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), suppress the hypothalamic-pituitary-thyroid (HPT) axis, reducing TSH secretion and thyroid hormone synthesis (Boelen et al., 2011). Peripheral metabolism of thyroid hormone is also altered, with decreased conversion of T4 to T3 via type 1 deiodinase and increased activity of type 3 deiodinase, which inactivates T4 and T3 (Fliers et al., 2015). This results in low circulating T3 levels, which can be energy-sparing in acute illness but can also continue into chronic critical illness, when diagnosis becomes difficult (Van den Berghe, 2014).

Distinguishing between NTIS and true hypothyroidism is an important diagnostic challenge, as both conditions may present with low FT3 and FT4. However, NTIS is typically followed by normal or low TSH, whereas hypothyroidism is characterized by elevated TSH (Warner & Beckett, 2010). Clinical context takes precedence: NTIS is associated with acute or chronic severe illness, whereas hypothyroidism may be pre-existing or precipitated by illnesses like iodine deficiency or amiodarone therapy (Fliers et al., 2015). Thyroid hormone replacement in NTIS is not indicated, as evidence suggests that it can exacerbate catabolism and mortality in critically ill patients (Brent & Hershman, 1986). However, in

individuals with known hypothyroidism, cautious continuation of levothyroxine may be warranted (Warner & Beckett, 2010).

Diagnosis strategies include scrutiny of the temporal pattern of illness, serial TFTs to monitor trends, and taking into consideration clinical factors like infection or organ dysfunction (Van den Berghe, 2014). For example, low FT3 with normal TSH in a septic patient most likely indicates NTIS, whereas recurrently elevated TSH is suggestive of hypothyroidism (Fliers et al., 2015). Additional tests, such as levels of reverse T3 (rT3), can support the diagnosis because elevated rT3 is characteristic of NTIS due to increased type 3 deiodinase activity (Boelen et al., 2011).

Biotin Interference

Biotin, a water-soluble B vitamin, is increasingly implicated in TFT misinterpretation by interfering with biotin-based immunoassays, which are widely used to measure TSH, FT4, and FT3 (Elston et al., 2016). High-dose biotin supplements taken for cosmetic purposes (e.g., nail and hair growth) or for medical conditions (e.g., multiple sclerosis) cause spurious elevations in FT4 and FT3 levels or spurious suppression of TSH, mimicking hyperthyroidism (Wijeratne et al., 2012). The use of biotin has become widespread, with over-the-counter supplements available in doses as high as 10 mg, well above the 30 µg daily recommended intake (Li et al., 2017).

Biotin interference is seen because most TFT immunoassays use biotin-streptavidin technology, in which exogenous biotin interferes with assay reagents, causing inaccurate results (Holmes et al., 2017; Batista et al., 2017). For example, in competitive FT4 and FT3 assays, high biotin levels result in falsely elevated results, while in sandwich TSH assays, biotin affects signal detection and leads to falsely depressed TSH (Elston et al., 2016). This may lead to a false diagnosis of hyperthyroidism with a risk of inappropriate treatments like antithyroid drugs or radioactive iodine (Wijeratne et al., 2012).

Prevention of biotin interference includes taking a good patient history for supplement use. Biotin withholding for 48–72 hours tends to eliminate interference, but high doses (e.g., 100 mg) may take up to 7 days to clear (Thienpont et al., 2010). Alternate assays, e.g., LC-MS/MS, not biotin-dependent, may confirm TFT results in suspected cases (Avery, 2019). Clinicians should also be aware of assay-specific vulnerability because not all TFT platforms are impacted equally (Elston et al., 2016). The key diagnostic aids in these circumstances are summarized in the following tables. Table 1 provides trimester-specific reference ranges for TFTs in pregnancy, essential for their correct interpretation. Table 2 and Figure 2 provide a diagnostic approach and management of NTIS and biotin interference, emphasizing clinical context and assay selection.

Table 1. Trimester-Specific Reference Ranges for Thyroid Function Tests in Pregnancy

Trimester	TSH (mIU/L)	FT4 (pmol/L)	FT3 (pmol/L)	Source
First	0.1–2.5	10–22	3.8–6.0	Alexander et al. (2017)
Second	0.2–3.0	9–18	3.2–5.5	Soldin et al. (2004)
Third	0.3–3.0	8–15	3.0–5.0	Laurberg et al. (2011)

Table 2. Diagnostic Considerations for NTIS and Biotin Interference

Scenario	TFT Pattern	Diagnostic Approach	Management Strategy	Source
NTIS	Low FT3, normal/low FT4, normal/low TSH	Assess clinical context, repeat tests, consider rT3	Avoid thyroid hormone replacement	Fliers et al. (2015)
Biotin Interference	High FT4/FT3, low TSH	Inquire about biotin use, discontinue 48–72h, use non-biotin assays	Confirm with LC-MS/MS, educate patients	Elston et al. (2016)

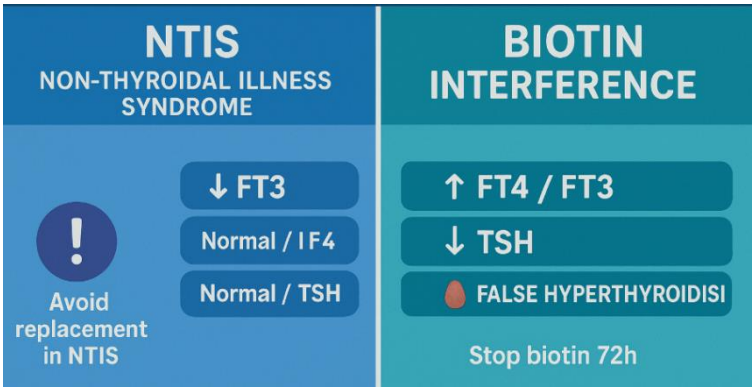

Figure 2. Comparative Patterns of Thyroid Function Tests in NTIS and Biotin Interference.

Discussion

Interpretation of thyroid function tests (TFTs) in difficult clinical circumstances, such as pregnancy, critical illness, and biotin interference, is extremely challenging due to physiological adaptations and analytical interferences that can potentially obscure true thyroid status. This review emphasizes the absolute importance of tailored approaches to TFT interpretation in order to avoid misdiagnosis and enable appropriate clinical management. Every circumstance—pregnancy, non-thyroidal illness syndrome (NTIS), and biotin interference—requires an understanding of underlying mechanisms, careful selection of investigative modalities, and rigorous adherence to evidence-based guidelines.

In pregnancy, physiological changes incited by increased estrogen, human chorionic gonadotropin (hCG), and thyroid-binding globulin (TBG) have a significant effect on TFT profiles, and trimester-specific reference ranges are essential to prevent misdiagnosis (Jonklaas et al., 2014). For instance, hCG's thyroid-stimulating activity in the first trimester can suppress TSH, mimicking hyperthyroidism, and the increase in TBG makes interpretation challenging by elevating total T4 and T3 concentrations, whereas free hormone levels are difficult to interpret (Glinoer, 1997; Laurberg et al., 2011). Avoidance of inappropriate interventions can be made by not using trimester-specific ranges, such as the unwarranted treatment of subclinical hypothyroidism, which could potentially harm patients without apparent advantages (Maraka et al., 2016). ATA recommendations emphasize trimester-specific TSH cutoffs (e.g., 0.1–2.5 mIU/L in the first trimester) and rigorous assays like liquid chromatography-tandem mass spectrometry (LC-MS/MS) for precise FT4 and FT3 measurements (Alexander et al., 2017; Saud Faleh Alanazi, 2024). Maternal risk factors must also be considered by clinicians, such as autoimmune thyroid disease, which increases the risk of hypothyroidism and also of adverse outcomes like miscarriage or preterm delivery (Krassas et al., 2010). It requires the integration of clinical history, antibody status (e.g., anti-thyroid peroxidase antibodies), and serial TFT monitoring to separate physiological from pathological processes.

Critical illness complicates matters through NTIS, whereby TFT abnormalities—low FT3, normal or low FT4, and normal or low TSH—are an adaptive response to systemic stress and do not represent true thyroid dysfunction (Fliers et al., 2015). NTIS is seen in conditions like sepsis, trauma, and organ failure and is present in as many as 70% of intensive care patients (Van den Berghe, 2014). The challenge lies in the distinction of NTIS from true hypothyroidism because both may present with low FT3 and FT4. NTIS, however, typically presents with normal or low TSH, whereas hypothyroidism presents with elevated TSH (Warner & Beckett, 2010). Replacement with thyroid hormone in NTIS is generally not advised because studies show it worsens catabolism and mortality (Brent & Hershman, 1986). Investigation plans include the assessment of clinical context, repeated TFTs to assess trends, and other markers like reverse T3 (rT3), which is elevated in NTIS via increased activity of type 3 deiodinase (Boelen et al., 2011). Clinicians must also exercise caution in patients with pre-existing thyroid disease, where continuation of levothyroxine may be indicated, according to clinical judgment and serial investigations (Warner & Beckett, 2010).

Biotin interference, increasingly common, is due to widespread consumption of high-dose biotin supplements, which interfere with biotin-based immunoassays, leading to falsely elevated FT4 and FT3 or falsely suppressed TSH, mimicking hyperthyroidism (Elston et al., 2016). Biotin consumption is now widespread, with over-the-counter availability of supplements in doses as high as 10 mg, far above the 30-µg daily requirement (Li et al., 2017). Such interference can lead to serious diagnostic errors, such as the institution of antithyroid therapy for alleged hyperthyroidism (Wijeratne et al., 2012). Mitigating strategies include obtaining a careful patient history for biotin use, withholding supplements for 48–72 hours (or longer in cases of high doses), and using non-biotin-based assays like LC-MS/MS for confirmation (Holmes et al., 2017; Trambas et al., 2016). Collaboration among laboratories is necessary to identify assay-specific weaknesses and implement appropriate testing strategies.

Conclusion

Accurate interpretation of thyroid function tests (TFTs) in difficult clinical situations—pregnancy, critical illness, and biotin interference—requires a keen understanding of physiological alterations, recognition of analytical pitfalls, and use of evidence-based diagnostic strategies. In pregnancy, trimester-specific reference ranges for TSH, FT4, and FT3 are required to account for physiological adjustments secondary to hCG, estrogen, and TBG, which can mimic thyroid dysfunction (Alexander et al., 2017; Glinoer, 1997). Failure to use these ranges can lead to overdiagnosis of disorders like subclinical hypothyroidism, with risks of inappropriate treatment or lack of treatment of true thyroid disease that can impact maternal and fetal health (Krassas et al., 2010; Madkhali et al., 2024).

In critical illness, non-thyroidal illness syndrome (NTIS) is a diagnostic challenge because its TFT profile of low FT3, normal or low FT4, and normal or low TSH can resemble hypothyroidism (Fliers et al., 2015). NTIS should be differentiated from true thyroid dysfunction because thyroid hormone replacement is generally contraindicated in NTIS but may be necessary in individuals with pre-existing hypothyroidism (Van den Berghe, 2014;

Warner & Beckett, 2010). Biotin interference, which is driven by the increasing popularity of high-dose supplements, disrupts TFT immunoassays, necessitating careful patient history, supplement cessation, and use of non-biotin-based assays like LC-MS/MS to confirm results (Elston et al., 2016; Holmes et al., 2017). By emphasizing trimester-specific ranges, conservative NTIS management, and proactive curtailment of biotin interference, it is intended to maximize diagnostic accuracy and improve patient outcomes in these challenging clinical scenarios

References

1. Alexander, E. K., Pearce, E. N., Brent, G. A., Brown, R. S., Chen, H., Dosiou, C., ... & Sullivan, S. (2017). 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid*, *27*(3), 315-389. https://doi.org/10.1089/thy.2016.0457
2. Aljehani, M. R., & Alhayek , A. A. (2024). Renal Function Assessment: Core Responsibilities of Clinical Pathologists and Laboratory Technicians in Diagnostic Evaluation. *Saudi Journal of Medicine and Public Health*, *1*(1), 65–74. https://doi.org/10.64483/jmph-39
3. Avery, G. (2019). Biotin interference in immunoassay: a review for the laboratory scientist. *Annals of clinical biochemistry*, *56*(4), 424-430. https://doi.org/10.1177/0004563219842231
4. Barbesino, G. (2016). Misdiagnosis of Graves' disease with apparent severe hyperthyroidism in a patient taking biotin megadoses. *Thyroid*, *26*(6), 860-863. https://doi.org/10.1089/thy.2015.0664
5. Batista, M. C., Ferreira, C. E., Faulhaber, A. C., Hidal, J. T., Lottenberg, S. A., & Mangueira, C. L. (2017). Biotin interference in immunoassays mimicking subclinical Graves' disease and hyperestrogenism: a case series. *Clinical Chemistry and Laboratory Medicine (CCLM)*, *55*(6), e99-e103. https://doi.org/10.1515/cclm-2016-0628
6. Boelen, A., Kwakkel, J., & Fliers, E. (2011). Beyond low plasma T3: local thyroid hormone metabolism during inflammation and infection. *Endocrine reviews*, *32*(5), 670-693.
7. Brent, G. A., & Hershman, J. M. (1986). Thyroxine therapy in patients with severe nonthyroidal illnesses and low serum thyroxine concentration. *The Journal of Clinical Endocrinology & Metabolism*, *63*(1), 1-8. https://doi.org/10.1210/jcem-63-1-1
8. Casey, B. M., & Leveno, K. J. (2006). Thyroid disease in pregnancy. *Obstetrics & Gynecology*, *108*(5), 1283-1292. *DOI:* 10.1097/01.AOG.0000244103.91597.c5
9. De Groot, L., Abalovich, M., Alexander, E. K., Amino, N., Barbour, L., Cobin, R. H., ... & Sullivan, S. (2012). Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*, *97*(8), 2543-2565. https://doi.org/10.1210/jc.2011-2803
10. Elston, M. S., Sehgal, S., Du Toit, S., Yarndley, T., & Conaglen, J. V. (2016). Factitious Graves' disease due to biotin immunoassay interference—a case and review of the literature. *The Journal of Clinical Endocrinology & Metabolism*, *101*(9), 3251-3255. https://doi.org/10.1210/jc.2016-1971
11. Fathi-Karkan, S., Sargazi, S., Shojaei, S., Far, B. F., Mirinejad, S., Cordani, M., ... & Ghavami, S. (2024). Biotin-functionalized nanoparticles: an overview of recent trends in cancer detection. *Nanoscale*, *16*(27), 12750-12792. https://doi.org/10.1039/D4NR00634H
12. Feldt-Rasmussen, U., & Rasmussen, Å. K. (2010). Autoimmunity in differentiated thyroid cancer: significance and related clinical problems. *Hormones*, *9*(2), 109-117. https://doi.org/10.14310/horm.2002.1261
13. Fliers, E., Bianco, A. C., Langouche, L., & Boelen, A. (2015). Thyroid function in critically ill patients. *The lancet Diabetes & endocrinology*, *3*(10), 816-825. https://doi.org/10.1016/S2213-8587(15)00225-9
14. Garber, J. R., Cobin, R. H., Gharib, H., Hennessey, J. V., Klein, I., Mechanick, J. I., ... & Woeber, K. A. (2012). Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocrine practice*, *18*(6), 988-1028. https://doi.org/10.4158/EP12280.GL
15. Glinoer, D. (1997). The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. *Endocrine reviews*, *18*(3), 404-433.
16. Haddow, J. E., Palomaki, G. E., Allan, W. C., Williams, J. R., Knight, G. J., Gagnon, J., ... & Klein, R. Z. (1999). Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *New England Journal of Medicine*, *341*(8), 549-555. DOI: 10.1056/NEJM199908193410801
17. Hazazi, Y. O. (2025). Strengthening Postpartum Depression Screening and Treatment within Primary Healthcare Centers in Riyadh 1st Cluster. *Saudi Journal of Medicine and Public Health*, *2*(2), 105–113. https://doi.org/10.64483/jmph-56
18. Holmes, E. W., Samarasinghe, S., Emanuele, M. A., & Meah, F. (2017). Biotin interference in clinical immunoassays: a cause for concern. *Archives of pathology & laboratory medicine*, *141*(11), 1459-1460. https://doi.org/10.5858/arpa.2017-0107-LE

19. Jonklaas, J., Bianco, A. C., Bauer, A. J., Burman, K. D., Cappola, A. R., Celi, F. S., ... & Sawka, A. M. (2014). Guidelines for the treatment of hypothyroidism: prepared by the american thyroid association task force on thyroid hormone replacement. *thyroid*, *24*(12), 1670-1751. https://doi.org/10.1089/thy.2014.0028
20. Krassas, G. E., Poppe, K., & Glinoer, D. (2010). Thyroid function and human reproductive health. *Endocrine reviews*, *31*(5), 702-755. https://doi.org/10.1210/er.2009-0041
21. Kwakkel, J., Fliers, E., & Boelen, A. (2011). Illness-induced changes in thyroid hormone metabolism: focus on the tissue level. *Neth J Med*, *69*(5), 224-8.
22. Laurberg, P., Andersen, S. L., Hindersson, P., Nohr, E. A., & Olsen, J. (2016). Dynamics and predictors of serum TSH and fT4 reference limits in early pregnancy: a study within the Danish National Birth Cohort. *The Journal of Clinical Endocrinology & Metabolism*, *101*(6), 2484-2492. https://doi.org/10.1210/jc.2016-1387
23. Li, D., Radulescu, A., Shrestha, R. T., Root, M., Karger, A. B., Killeen, A. A., ... & Burmeister, L. A. (2017). Association of biotin ingestion with performance of hormone and nonhormone assays in healthy adults. *Jama*, *318*(12), 1150-1160. doi:10.1001/jama.2017.13705
24. Maraka, S., Ospina, N. M. S., O'Keeffe, D. T., Espinosa De Ycaza, A. E., Gionfriddo, M. R., Erwin, P. J., ... & Montori, V. M. (2016). Subclinical hypothyroidism in pregnancy: a systematic review and meta-analysis. *Thyroid*, *26*(4), 580-590. https://doi.org/10.1089/thy.2015.0418
25. Madkhali, A. M., Bouri, H. A., Alotaibi, F. O. E., ALMUTAIRI, A. M. M., Albalawi, T. suliman, Alotaibi, G. S., … Alotaibi, A. S. (2024). Potential Health Implications of Fifth Generation (5G) Wireless Communication Technology: A Review of Emerging Biological and Epidemiological Concerns. *Saudi Journal of Medicine and Public Health*, *1*(1), 94–105. https://doi.org/10.64483/jmph-53
26. Sahib, N. A. H. F., & Mohammed, K. G. (2024). Evaluation of Anti-Thyroglobulin, Anti-Thyroid Peroxidase Autoantibodies and Thyroid Stimulating Hormone in Autoimmune Thyroiditis Patients. *Medical Science Journal for Advance Research*, *5*(4). https://doi.org/10.46966/msjar.v5i4.205
27. Saud Faleh Alanazi. (2024). Comparative Evaluation of the Pharmacological Mechanisms, Clinical Indications, and Risk Management Strategies of Epidural Anesthesia in Surgical and Obstetric Interventions. Saudi Journal of Medicine and Public Health, *1*(1), 47–57. https://doi.org/10.64483/jmph-36
28. Soh, S. B., & Aw, T. C. (2019). Laboratory testing in thyroid conditions-pitfalls and clinical utility. *Annals of laboratory medicine*, *39*(1). https://doi.org/10.3343/alm.2019.39.1.3
29. Soldin, O. P., Tractenberg, R. E., Hollowell, J. G., Jonklaas, J., Janicic, N., & Soldin, S. J. (2004). Trimester-specific changes in maternal thyroid hormone, thyrotropin, and thyroglobulin concentrations during gestation: trends and associations across trimesters in iodine sufficiency. *Thyroid*, *14*(12), 1084-1090. https://doi.org/10.1089/thy.2004.14.1084
30. Surks, M. I., Ortiz, E., Daniels, G. H., Sawin, C. T., Col, N. F., Cobin, R. H., ... & Weissman, N. J. (2004). Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *Jama*, *291*(2), 228-238. doi:10.1001/jama.291.2.228
31. Thienpont, L. M., Van Uytfanghe, K., Beastall, G., Faix, J. D., Ieiri, T., Miller, W. G., ... & IFCC Working Group on Standardization of Thyroid Function Tests. (2010). Report of the IFCC Working Group for Standardization of Thyroid Function Tests; part 2: free thyroxine and free triiodothyronine. *Clinical Chemistry*, *56*(6), 912-920. https://doi.org/10.1373/clinchem.2009.140194
32. Trambas, C. M., Sikaris, K. A., & Lu, Z. X. (2016). More on biotin treatment mimicking Graves' disease. *The New England journal of medicine*, *375*(17), 1698. https://doi.org/10.1056/nejmc1611875
33. Van den Berghe, G. (2014). Non-thyroidal illness in the ICU: a syndrome with different faces. *Thyroid*, *24*(10), 1456-1465. https://doi.org/10.1089/thy.2014.0201
34. Vassiliadi, D. A., Ilias, I., Pratikaki, M., Jahaj, E., Vassiliou, A. G., Detsika, M., ... & Dimopoulou, I. (2021). Thyroid hormone alterations in critically and non-critically ill patients with SARS-CoV-2 infection. *Endocrine connections*, *10*(6), 646-655. https://doi.org/10.1530/EC-21-0029
35. Warner, M. H., & Beckett, G. J. (2009). Mechanisms behind the non-thyroidal illness syndrome: an update. *The Journal of endocrinology*, *205*(1), 1-13. https://doi.org/10.1677/joe-09-0412