Hypothyroidism in Clinical Practice

Faiza Qari

Consultant Endocrinologist, King Abdulaziz University, Jeddah, Saudi Arabia

Abstract

Background: Hypothyroidism is the most common endocrine disease that was seen in the clinical practice especially for family physicians. **Methods:** This review article covered the important practical clinical issues for managing overt hypothyroidism, subclinical hypothyroidism and hypothyroidism during pregnancy. **Conclusions:** The clinical issues were addressed by clinical scenario followed by questions and stressed on the important clinical points.

Keywords: Hypothyroidism, subclinical hypothyroidism, hypothyroidism during pregnancy

What issues about hypothyroidism should be covered in clinical practice?

- *Underlying causes* — The most common cause of primary hypothyroidism is autoimmune thyroiditis. Hashimoto's thyroiditis is the combination of autoimmune thyroiditis and goiter; a positive test result for thyroid auto antibodies (antithyroglobulin and antiperoxidase) will confirm the diagnosis.
- *Current and previous drug use* — Check for history of thyroid surgery or head and neck irradiation and radioactive iodine therapy for thyrotoxicosis.[1]
- *Menstrual and obstetric history* — Check for a history of amenorrhea and menorrhagia.
- *Examination* of the neck for presence or absence of goiter or a thyroidectomy scar. Also examine for general features of hypothyroidism and associated organ-specific autoimmune diseases such as vitiligo.[2]

What are the important issues in treating hypothyroidism?

- Prescribe oral thyroxin 50-100 g daily. The initial dose in old patients with ischemic heart disease should be 25 g daily.[3]
- Monitor treatment with tests of serum TSH concentrations.
- Change the thyroxin dosage by 26-50 g daily. Then measure the TSH concentration 4-6 weeks later until the TSH has normalized.
- Once euthyroidism is achieved, patients should be monitored annually by measuring the level of TSH to ensure that thyroxin replacement is adequate.[4]

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/2249-4863.137609

- Explain that treatment is likely to be lifelong with minimal side effects if administered at the correct dosage and that the prognosis is excellent.[5]
- Tell the patient that it may take a few weeks for thyroxin to begin working and that he/she should not expect all symptoms to disappear within a few days of starting treatment.[6,7]

What are the causes of persistently elevated TSH despite adequate hormone replacement?

- Poor compliance is the most common reason for continued elevation of the TSH level in patients receiving presumably adequate thyroid hormone replacement. Patients who do not regularly take their replacement medication and then try to "catch up" just before physician visit may restore their FT4 levels to normal but continue to have an elevated TSH level.

A number of medications and diseases alter thyroid hormone replacement requirements

A: - Drugs that increase replacement requirements".[8]

i) Drugs that reduce thyroid hormone production
   - Lithium
   - Iodine-containing medications
   - Amiodarone (Cordarone®)
   - Drugs that reduce thyroid hormone absorption
   - Sucralfate (Carafate®)
   - Ferrous sulfate (slow iron)
   - Cholestyramine (Questran®)
   - Colestipol (Colestid®)
   - Aluminum-containing antacids
   - Calcium products

Address for correspondence: Prof. Faiza Qari, Consultant Endocrinologist, King Abdulaziz University, P.O. Box 13042, Jeddah 21943, Saudi Arabia.
E-mail: faizaqari@gmail.com

i) Drugs that increase metabolism of thyroxine
   - Rifampin (Rifadin®)
   - Phenobarbital
   - Carbamazepine (Tegretol®)
   - Warfarin (Coumadin®)
   - Oral hypoglycemic agents

B: - Increase thyroxin availability and may decrease replacement requirements

i) Drugs that displace thyroid hormone from protein binding
   - Furosemide (Lasix®)
   - Mefenamic acid (Ponstel®)
   - Salicylates

Adapted with permis.

Coexisting diseases[9]

Diseases causing malabsorption, e.g., celiac disease, tropical sprue and previous small intestine surgery.

Conditions associated with reduced gastric acid production.

H. pylori infection

Increased thyroxin clearance (coexisting conditions)

- Pregnancy, nephritic syndrome

Subclinical hypothyroidism in clinical practice

A 36-year-old woman is found to have a serum TSH level of 7 mU/L on routine screening. Her only symptoms are mild fatigue, which has been present for more than 2 years, and difficulty in losing weight.

What are the issues about subclinical hypothyroidism that should be covered in clinical practice?

- Subclinical hypothyroidism occurs in the clinical setting of a serum TSH level above the upper limit of normal despite a normal serum FT4 concentration.
- Initiating levothyroxine (LT4) replacement therapy is recommended for all patients with a TSH level greater than 10 mIU/L, even if the FT4 concentration is within normal laboratory range.
- However, treatment of patients with serum TSH levels between 5 and 10 mIU/L remains controversial. The strongest arguments for LT4 therapy are the high risk of progression to overt hypothyroidism. The possible improvement of quality of life, lipid abnormalities, adverse cardiac end points, cardiac dysfunction, adverse fetal effects and pregnancy outcomes, possible contribution to infertility, neuromuscular dysfunction, psychiatric dysfunction, and cognitive dysfunction. Several investigators have demonstrated that subclinical hypothyroidism is a cardiovascular risk factor. Although subtle, the clinical significance is debatable. To date, studies have not shown an association of subclinical hypothyroidism with cardiac events and cardiovascular mortality.[10]

What are the risks of not treating subclinical hypothyroidism?

- Increased risk of heart attack and atherosclerosis.[11]
- Increased risk of elevated cholesterol and high triglycerides.[12]
- Increased risk of depression, anxiety, and panic attacks.[13]
- Increased risk of miscarriage.

Increased risk of developmental delays in infants born to mothers who were sub".

- Clinically hypothyroid during pregnancy.[14]

What are the indications for treating subclinical hypothyroidism?

- Individuals with serum TSH levels between 5 and 10 mIU/L should be treated selectively.[15]
- Thyroxin replacement therapy should be reserved for patients who have goiter, women who are anticipating pregnancy or are pregnant, or patients with depression or bipolar disorder. Subclinical hypothyroidism associated with autoimmune thyroiditis in children and adolescents should be treated.[16]

Hypothyroidism and pregnancy

A 36-year-old woman who was diagnosed with hypothyroidism 3 years ago tells her endocrinologist that she wants to conceive in the next year. She was treated with LT4, 0.1 mg daily. Her last serum TSH was 0.7 mIU/L. She is instructed to notify her endocrinologist as soon as she finds out that she is pregnant so that a serum TSH level can be checked. Her menstrual period is 1 week late, a home pregnancy test is positive, and her serum TSH level is 1.9 mIU/L.

What issues about hypothyroidism during pregnancy should be covered in clinical practice?

The prevalence of hypothyroidism during pregnancy is 2.5%, with the most frequent form being subclinical hypothyroidism. The most common cause of hypothyroidism in women of reproductive age is AITD (Hashimoto's hypothyroidism). A history of total or subtotal thyriodoectomy, radioiodine ablation, or transient thyroiditis accounts for most of the remaining cases of hypothyroidism in pregnant women.[17]

Risks of hypothyroidism to the fetus

- Preterm delivery has been found to be three-fold more common in hypothyroid pregnant women and has also been associated with an increase in spontaneous abortions, fetal death, placental abruption, preterm delivery, and postpartum hemorrhage.
- Another worrying danger associated with maternal hypothyroidism (especially when present during the first trimester) is the adverse consequence to child neuropsychointellectual development. A seminal study by Haddow *et al.*[18] showed a 7-point reduction in intelligence

quotient in children aged 7 to 9 years whose mothers had subclinical hypothyroidism pregnancy compared with the children of euthyroid mothers.[19]

Screening of hypothyroidism during pregnancy

Documentation of an elevated serum TSH level confirms the diagnosis of primary hypothyroidism. The presence of thyroid auto antibodies (Tabs) is a useful confirmatory finding. Serum TSH>2.5mU/L in pregnant women should be used as a guide for thyroid dysfunction. If the serum TSH is >4 mU/L irrespective of the presence (or absence) of TAbs, there is no doubt about the existence of hypothyroidism during pregnancy.

The American Association of Clinical Endocrinologists advises that all pregnant women be screened for thyroid problems. They recommend, specifically, the following:

- Anyone considering becoming pregnant should have her thyroid checked in advance.
- All pregnant women with a family history or symptoms of a thyroid disease should be tested.[20]

A disadvantage of screening during pregnancy is of course that the fetal brain is dependent on maternal T4 from conception and by the time testing is possible (probably at the booking antenatal visit at around 14 weeks), damage may already have occurred.[21] Nevertheless, maternal T4 is still an important source of thyroid hormone for the fetal brain during the rest of the pregnancy.[22]

What are the important issues in treating hypothyroid pregnant women?

- Prevention of hypothyroidism: Adequate iodine supplementation is crucial to preventing maternal hypothyroidism. Fertile women with normally functioning thyroid glands should have an average iodine intake of 150 mg/day. During pregnancy and breastfeeding, women should increase their iodine intake to 250 mg daily.[23]
- Hypothyroid pregnant women already on LT4 replacement therapy will require a dose increase from 25% to 50% on average to maintain desirable TSH level < 2.5 mIU/L during pregnancy because they have inadequate thyroid reserve. Most hypothyroid pregnant women need a dose increase during the first trimester. In the second trimester, there is generally a plateau in LT4 requirements, but 25-40% of women may need a further dose increase during the third trimester. The increase is at least partly dependent on the thyroid reserve of the patient but also the size of the distribution space and the number of babies. Therefore, women with a history of total thyriodoectomy will be most dependent. Generally, patients with ongoing Hashimoto's thyroiditis require a 25% increase in LT4 dose, whereas the increase is more likely to be 50% in women with total thyriodctomy. Adjustments of the thyroxin dose are made by increasing LT4 by 25-50 mg/day. Serum TSH and FT4 should always be evaluated 3-4 weeks after every change of dosage.[24] Possible LT4 interactions with coexisting diseases such as gastritis, or medications such as iron supplements, calcium, vitamins, or omeprazole, may reduce LT4 absorption. It is best to advise a 4-hour delay between the medications and LT4 and to take the LT4 on empty stomach.
- Postpartum: After delivery, LT4 dosing generally can be returned to pre-pregnancy requirements.

Levothyroxine and breastfeeding

The quantity of thyroid hormone transferred into human milk is too low to affect plasma thyroid hormone levels in neonates. The American Academy of Pediatrics considers LT4 compatible with breastfeeding and has reported that no observable change is seen in nursing infants whose mothers are taking LT4.[25]

References

1. Lindsay RS, Toft AD. Hypothyroidism. Lancet 1997;349:413-6.
2. Topliss DJ, Eastman CJ. Diagnosis and management of hyperthyroidism and hypothyroidism. Med J Aust 2004;180:186-93.
3. Wallace K, Hoffman MT. Thyroid dysfunction: How to manage overt and subclinical disease in older patients. Geriatrics 1998;53:32-8,41.
4. Hueston WJ. Treatment of Hypothyroidism Am Fam Physician 2001;64:1717-24.
5. Singer PA, Cooper DS, Levy EG, Ladenson PW, Braverman LE, Daniels G, *et al.* Treatment guidelines for patients with hyperthyroidism and hypothyroidism. Standards of Care Committee, American Thyroid Association. JAMA 1995;273:808-12.
6. Khandelwal D, Tandon N. Overt and subclinical hypothyroidism: Who to treat and how. Drugs 2012 1;72:17-33.
7. Neves C, Alves M, Medina JL, Delgado JL. Thyroid diseases, dyslipidemia and cardiovascular pathology. Rev Port Cardiol 2008;27:1211-36.
8. Surks MI, Sievert R. Drugs and thyroid function. N Engl J Med 1995;333:1688-94.
9. Ward LS. The difficult patient: drug interaction and the influence of concomitant diseases on the treatment of hypothyroidism. Arq Bras Endocrinol Metabol. 2010;54:435-42.
10. Fatourechi V. Subclinical hypothyroidism: An update for primary care physicians. Mayo Clin Proc 2009;84:65-71.
11. Duntas LH, Wartofsky L. Cardiovascular risk and subclinical hypothyroidism: Focus on lipids and new emerging risk factors: What is the evidence? Thyroid 2007;17:1075-84.
12. Meier C, Staub JJ, Roth CB, Guglielmetti M, Kunz M, Miserez AR, *et al.* TSH-controlled L-thyroxine therapy reduces cholesterol levels and clinical symptoms in subclinical hypothyroidism: A double blind, placebo-controlled trial (Basel Thyroid Study). J Clin Endocrinol Metab 2001;86:4860-6.
13. Haggerty JJ Jr, Garbutt JC, Evans DL, Golden RN, Pedersen C, Simon JS, *et al.* Subclinical hypothyroidism: A review of neuropsychiatric aspects. Int J Psychiatry Med 1990;20:193-208.
14. Klubo-Gwiezdzinska J, Burman KD, Van Nostrand D, Wartofsky L. Levothyroxine treatment in pregnancy: Indications, efficacy, and therapeutic regimen. J Thyroid Res 2011;2011:843591.
15. Fatourechi V, Lankarani M, Schryver PG, Vanness DJ, Long KH, Klee GG. Factors influencing clinical decisions to initiate

thyroxine therapy for patients with mildly increased serum thyrotropin (5.1-10.0 mIU/L). Mayo Clin Proc 2003;78:554-60.

16. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, *et al.* Subclinical thyroid disease: Scientific review and guidelines for diagnosis and management. JAMA 2004;291:228-38.
17. Okosieme OE, Marx H, Lazarus JH. Medical management of thyroid dysfunction in pregnancy and the postpartum. Expert Opin Pharmacother 2008;9:2281-9.
18. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, *et al.* Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341:549-55.
19. Menif O, Omar S, Feki M, Kaabachi N. Hypothyroidism and pregnancy: Impact on mother and child health. Ann Biol Clin (Paris) 2008;66:43-51.
20. Davies TF. Time for the American Thyroid Association to lead on thyroid screening in pregnancy. Thyroid 2007;17:697-8.
21. Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchison S, *et al.* Detection of thyroid dysfunction in early pregnancy: Universal screening or targeted high-risk case finding? J Clin Endocrinol Metab 2007;92:203-7.
22. Lazarus JH, Prema wardhana LD. Screening for thyroid disease in pregnancy. J Clin Pathol 2005;58:449-52.
23. Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, *et al.* Management of thyroid dysfunction during pregnancy and postpartum: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2007;92:S1-47.
24. Toft A. Increased levothyroxine requirements in pregnancy — Why, when, and how much? N Engl J Med 2004;351:292-4.
25. Smith VC, Svoren BM, Wolfsdorf JI. Hypothyroidism in a breast-fed preterm infant resulting from maternal topical iodine exposure. J Pediatr 2006;149:566-7.

How to cite this article: Qari F. Hypothyroidism in clinical practice. J Fam Med Primary Care 2014;3:98-101.

Source of Support: Nil. **Conflict of Interest:** None declared.