



GRAVES' DISEASE & THYROID FOUNDATION

*Educate * Encourage * Empower*

P.O. Box 2793 • Rancho Santa Fe, CA 92067 • (877) 643-3123 • www.gdatf.org • info@gdatf.org

Diagnosis and Treatment of Subclinical Hypothyroidism

by Cherie Lisa Vaz, MD
Assistant Professor
Endocrinology, Diabetes, & Metabolism
Temple University School of Medicine

With the widespread prevalence of autoimmune hypothyroidism, patients frequently have subclinical hypothyroidism, which is a possible predecessor to overt hypothyroidism. In the National Health and Examination Survey III the prevalence of subclinical hypothyroidism was 4.3 percent (1).

What is subclinical hypothyroidism?

Subclinical hypothyroidism is a milder form of hypothyroidism. Patients may be asymptomatic or have a few vague symptoms. Often, it is diagnosed on routine blood work when a thyroid function test is found to be abnormal. In fact, this disorder can only be confirmed on the basis of laboratory test results just as in the diagnosis of hypothyroidism or hyperthyroidism.

Diagnosis

Thyroid hormones typically measured are free thyroxine; 'FT4', total

triiodothyronine; 'T3' and thyroid stimulating hormone 'TSH'; which is released from the pituitary gland. TSH begins to rise when the pituitary gland recognizes that there is deficient supply of thyroid hormone. Subclinical hypothyroidism is diagnosed if only the TSH level is elevated more than the upper limit of normal which is typically around 4.5mIU/l but the measured circulating thyroid hormones (FT4 and T3) fall in the normal range. Most patients with serum TSH <10 mU/L are asymptomatic. The typical pattern of laboratory tests for subclinical hypothyroidism may be different in case of pituitary disease where TSH production is affected. In case of pituitary tumors with subclinical hypothyroidism blood tests may show a low, inappropriately normal, or mildly elevated TSH.

Causes

Causes of subclinical hypothyroidism are similar

to those of hypothyroidism. The most common cause is autoimmune thyroid disease. Patients with a family history of autoimmune thyroid disease have a higher risk for developing subclinical and overt hypothyroidism. Subclinical hypothyroidism may occur after any form of thyroid injury such as following a partial thyroidectomy for a thyroid nodule or radioactive iodine therapy for hyperthyroidism. Drugs which impair thyroid function like iodine and iodine-containing medications could induce hypothyroidism which may be subclinical to begin with. It can also occur in case of pituitary tumors and some rarer genetic diseases like TSH receptor gene mutations.

Symptoms and Signs

With advancing age, subclinical hypothyroidism may be even more common as TSH does tend to rise with age and typically presents with milder

symptoms in older people. One may present with mild non-specific symptoms of hypothyroidism, such as fatigue, constipation and depression. A mild thyroid gland enlargement or goiter may be seen. In some studies treatment with thyroid hormone was associated with a significant decrease in goiter in cases of subclinical hypothyroidism (2). However this is not uniformly applicable to all patients and many goiters do not shrink with thyroid hormone replacement. Cognitive benefit from treating subclinical hypothyroidism is variable with some studies showing benefit while others not (3).

Effects of subclinical hypothyroidism and benefits of its treatment on cardiovascular disease is a controversial topic and more research is needed in this area before formal recommendations are made (4, 3). Large prospective clinical trials are needed to assess whether thyroid hormone replacement improves cardiovascular outcomes in patients with subclinical hypothyroidism. We do have evidence from several randomized clinical trials showing improvement of lipid (cholesterol) parameters in patients with subclinical hypothyroidism with thyroid hormone treatment. Serum total and LDL cholesterol decreased significantly with thyroid hormone replacement (5,

6). Importantly, these trials included patients with serum TSH concentrations >10 mIU/L. Similarly, trials in patients with TSH < 10 mIU/L did not show significant benefits on the lipid panel with thyroid hormone replacement (4). Thus patients with a higher TSH, usually >10 mIU/L are most likely to be symptomatic and more likely to benefit from treatment of subclinical hypothyroidism with thyroid hormone replacement.

Prognosis

Many patients with subclinical hypothyroidism eventually progress to overt hypothyroidism. Some factors which might suggest a higher risk of progression to overt hypothyroidism are the presence of anti-thyroid antibodies and high TSH levels > 12 mIU/L (7). The risk of developing hypothyroidism in women with positive antibodies and elevated TSH is around 4% per year versus 2%-3% per year with one risk factor only (3). Spontaneous recovery can occur in patients with subclinical hypothyroidism, but the frequency is unknown. Patients with lower TSH levels are most likely to have spontaneous recovery (7).

Treatment

Sometimes a laboratory test which suggests subclinical hypothyroidism is best repeated and may spontaneously normalize

over a period of 6 to 12 months. If patients have many symptoms suggestive of thyroid hormone deficiency, one may consider starting treatment with thyroid hormone to see if symptoms are possibly alleviated. However, replacing thyroid hormone in patients with subclinical hypothyroidism with modest elevations of TSH especially if $<8-10$ mIU/L is not always the best recommended approach, especially in elderly patients with heart arrhythmias or those at risk for arrhythmias, and in patients with osteoporosis. An individualized decision is made in each case and your doctor will discuss the risks and benefits of treatment in each case. Goal of treatment is to replace sufficient amount of thyroid hormone so as to reduce the TSH to within the normal range.

Subclinical hypothyroidism is always treated during pregnancy and preferably also when a patient is trying to conceive. Hypothyroidism in pregnancy is treated differently than in non-pregnant individuals. It is recommended you consult your endocrinologist as soon as you find out you are pregnant if you were previously told you have subclinical hypothyroidism.

The decision to treat subclinical hypothyroidism when the TSH is less than 10 mIU/L is based on the

individual patient presentation. Clinical symptoms and signs, other co-morbidities like cardiovascular disease, lipid abnormalities and osteoporosis are among the important factors to be considered when making this decision.

References

1. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, Braverman LE Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab.* 2002;87(2):489
2. Romaldini JH, Biancalana MM, Figueiredo DI, Farah CS, Mathias PC Effect of L-thyroxine administration on antithyroid antibody levels, lipid profile, and thyroid volume in patients with Hashimoto's thyroiditis. *Thyroid.* 1996;6(3):183.
3. AACE Clinical practice guidelines for Hypothyroidism in Adults *Thyroid.* 2013 Jan;23(1):129.
4. Villar HC, Saconato H, Valente O, Atallah AN Thyroid hormone replacement for subclinical hypothyroidism. *Cochrane Database Syst Rev.* 2007
5. Iqbal A, Jorde R, Figenschau Y Serum lipid levels in relation to serum thyroid-stimulating hormone and the effect of thyroxine treatment on serum lipid levels in subjects with subclinical hypothyroidism: the Tromsø Study. *J Intern Med.* 2006;260(1):53.
6. Caraccio N, Ferrannini E, Monzani F Lipoprotein profile in subclinical hypothyroidism: response to levothyroxine replacement, a randomized placebo-controlled study. *J Clin Endocrinol Metab.* 2002;87(4):1533.

7. Díez JJ, Iglesias P Spontaneous subclinical hypothyroidism in patients older than 55 years: an analysis of natural course and risk factors for the development of overt thyroid failure. *J Clin Endocrinol Metab.* 2004;89(10):4890.

© Copyright Graves' Disease & Thyroid Foundation. All rights reserved.

Used with permission of the author: Dr. Cherie Vaz