

Hypothyroidism In The Elderly

Tapas Das,¹ Arijit Ghosh, Anirban Sinha

¹Professor, Department of Medicine, Incharge Geriatric Clinic, IPGMER, SSKM Hospital, Kolkata

A. Definition

Hypothyroidism commonly results from an insidious process of thyroid failure and a state of decreased thyroid hormone availability of peripheral tissues but rarely it can be due to tissue unresponsiveness to the presence of adequate amounts of thyroid hormone in the circulation. Mild thyroid failure with an elevated serum TSH (Thyroid Stimulating Hormone) level and normal FT₄ (Free Thyroxine) concentration is referred to as subclinical hypothyroidism. The combination of a low serum FT₄ level and elevated serum TSH level together with clinical findings of hypothyroidism is defined as overt hypothyroidism.¹

B. Prevalence and Incidence

The prevalence of hypothyroidism varies based on the population under study, ethnicity and iodine content of the diet.¹

Among the patients admitted to a geriatric unit the prevalence of hypothyroidism is 2 – 7.4%.¹ In patients above 60 years of age in the general population the incidence of overt hypothyroidism is 2.3 – 10.3%.¹

In one review, the prevalence estimates of overt hypothyroidism have been stated to range from 0.5 – 5% and subclinical hypothyroidism from 5 – 20% of adults older than 60 years.²

In another study TSH levels more than 10 iU/ml. were found in 7% of women and 3% of men who were 60 to 89 years of age and living active lives in the community.³

C. Etiology and Pathogenesis

Primary hypothyroidism due to disease or dysfunction of thyroid gland itself accounts for 99% of the cases of hypothyroidism in elderly and indicates that the thyroid gland is unable to respond to TSH.

Secondary hypothyroidism resulting from

pituitary disease accounts for 1% of elderly with hypothyroidism, which is due to insufficient production or release of TSH.

In the elderly population the most common cause of primary hypothyroidism is chronic autoimmune thyroiditis (Hashimoto's disease).^{4,5}

Autoimmune thyroiditis is histologically characterised by continuous replacement of thyroid tissue with lymphocytic and fibrous tissue.^{6,7}

Many patients are identified by demonstrating the presence of anti-thyroglobulin and anti-microsomal antibodies in the serum.^{8,9,10}

The prevalence of positive thyroid antibodies increases with age with frequencies as high as 33% in women older than 70 years of age.¹

There is growing evidence of the presence of another family of immunoglobulin that are capable of blocking the action of TSH on thyroid cells either by interfering with TSH binding to its receptor or by blocking both pre and post-receptor processes, which results in shrinkage of the thyroid gland.¹¹

The **second** most common cause of primary hypothyroidism is treatment with radio-iodine and thyroid surgery (subtotal thyroidectomy) for Graves disease.^{12,13,14} In both situations, chances of developing hypothyroidism is upto 20 – 40% after one year and an annual risk of 2-4% thereafter.¹¹

About 20–47% of patients receiving radio therapy for various malignancies of the head and neck region also develop hypothyroidism which is a very slow process.¹

Iodide and iodine containing drugs can result in inhibition of thyroid hormone synthesis (Wolff–Chaikoff effect) with ensuing hypothyroidism which is usually reversible when the exogenous source of iodide or iodine is removed.¹⁵

Common sources of iodine ingestion are expectorants (potassium iodide), topical antifungal or antiseptic agents (betadine), iodine containing radiographic contrast agents, drugs like amiodarone and lithium.¹⁶

Amiodarone inhibits conversion of T₄ (Thyroxine) to T₃ (Tri-iodothyronine) peripherally and slows the metabolism of thyroxine. Frequency of developing hypothyroidism in United States is 10 – 20%.¹

20% of patients on chronic lithium therapy develop hypothyroidism due to impaired thyroid hormone synthesis and release.¹⁷

Recombinant interleukin-2A and recombinant IFN can precipitate hypothyroidism specially in patients with underlying autoimmune thyroiditis.^{18,19}

Iodine deficiency is also an important cause of hypothyroidism in many underdeveloped parts of the world.¹¹

Impairment of release of TRH (Thyrotrophin Releasing Hormone) from the hypothalamus leads to tertiary hypothyroidism.¹

D. Causes of hypothyroidism in elderly population¹

Primary hypothyroidism

Chronic autoimmune thyroiditis (Hashimoto's)
Radio-iodine therapy and radiation therapy for head and neck cancer
Surgical thyroidectomy
Drugs

Iodine containing drugs : Amiodarone,
Iodinated radiocontrast agents, Glycerol
Antithyroid drugs: Propyl thiouracil,
Carbimazole, Lithium

Iodine deficiency

Secondary hypothyroidism

Pituitary tumours
Pituitary surgery
Radiation
Hypothalamic tumours or granuloma

E. Clinical Manifestations

Hypothyroidism in older persons is a great masquerader: the symptoms are often attributed to 'old age' or to other disorders common in the elderly. The symptoms and signs emerge over many years so that neither the patient nor close associates may be aware of the process.^{20,21} If we bank upon the classical symptoms of hypothyroidism to detect an elderly hypothyroid we may miss a large number of cases.²² In one study only 10 percent of patients with laboratory confirmed diagnosis were recognized as being hypothyroid on clinical examination.²³

Central nervous system manifestations are a significant consequence of hypothyroidism in elderly population. Mental slowing, fatigability and excessive sleepiness are common. The possibility of psychiatric disorder is likely in patients who present with depression, delirium or paranoid ideas.^{24, 25, 26} So called myxedema madness is infrequent. An acute decline in mental status in the form of confusion and coma may be precipitated by stress of infection, trauma, cold, sedatives and narcotics.²⁷

Seizure may occur in severe hypothyroidism. Most reports confirm that while hypothyroidism is common with dementia only rarely is the dementia truly reversible with thyroid hormone therapy although there may be an overall improvement in the patient's functional status.²⁸

Entrapment neuropathy with paraesthesias can occur especially involving carpal tunnel.²⁸

The hung-up reflex may not be elicited because frequently there may be complete loss of reflexes or there may be hyporeflexia specially of the Achilles tendon in people over 65 years of age.¹¹

Evidence suggestive of myopathy may be due to very high CPK level. This may be largely attributed to decreased clearance of the enzyme.

Classical cold intolerance, diminished sweating, dry skin, puffiness of face, peri-orbital oedema, coarse skin and thinned hair, thinning of the outer part of the eyebrows are found with great frequency but at the same time these are not infrequent in the euthyroid elderly.¹⁹

In the elderly, assessment of changes in weight may give little insight into a possible diagnosis of hypothyroidism. Weight gain may occur but decrease in appetite may be sufficient to result in weight loss.

Constipation which is a common complaint is also a common problem in euthyroid elderly.¹¹

The myocardial involvement in hypothyroidism may result in bradycardia, decreased ventricular filling and impaired contractility. The myocardium may undergo myxoedematous infiltration with cardiomegaly, symptom of IHD and development of pericardial effusion. ECG abnormalities may include bradycardia, low voltage QRS complex, flattening or inversion of T waves and ventricular arrhythmia.²⁹

Anaemia is more readily detectable on laboratory evaluation. It is normocytic or macrocytic in type.³⁰ Serum iron may be low. Serum folic acid and Vit B₁₂ are normal.

Pernicious anaemia may co-exist with autoimmune hypothyroidism and should be looked for in hypothyroid patients with persistent anaemia after hormonal treatment or in patients with macrocytosis and low serum Vit B₁₂.

Hyponatremia occurs frequently in elderly hypothyroidism. Increased release of antidiuretic hormone (ADH) may give rise to Syndrome of Inappropriate Secretion of Anti – Diuretic Hormone (SIADH).¹¹

Myxoedema coma is a dreaded complication of untreated hypothyroidism in the elderly because of their increased susceptibility to comorbid illness, impaired thermoregulation and usage of sedatives, tranquilizers or narcotics.²⁷ It carries a mortality rate as high as 50%.¹¹

CLINICAL FEATURES OF HYPOTHYROIDISM IN ELDERLY¹

Cutaneous & metabolic

- Dry skin
- Hair loss
- Edema – peripheral, face and eyelids
- Cold intolerance
- Weight gain

Neurological

- Paraesthesia
- Ataxia
- Dementia

Psychiatric and behavioural disturbance

- Depression
- Apathy or withdrawal
- Psychosis
- Cognitive dysfunction

Musculoskeletal

- Myopathy
- Arthritis /Arthralgia

Cardiovascular

- Bradycardia
- Pericardial effusion
- Congestive heart failure

F. Subclinical Hypothyroidism In The Elderly

A significant population of individuals has been identified who have serum levels of TSH above the

accepted upper limits of normal and symptoms of hypothyroidism are usually mild or lacking.^{31, 32, 33} This syndrome is known as subclinical hypothyroidism and is most commonly found in women above the age of 60 years.^{34, 35}

In Framingham study 5.9% of subjects over the age of 60 years had clearly elevated serum TSH concentration of > 10 μ U/ml with normal serum T₄ levels and additional 14.4% had slightly elevated serum TSH (5 –10) μ U/ml with normal T₄.³⁶

What happens to patients who are found to have an elevated TSH level with out other findings ? In some cases the TSH level will be normal, measured again after several months. We would then attribute the initial elevation to laboratory error or perhaps to an episode of thyroiditis with a transient hypothyroid phase. In other cases, the subclinical hypothyroidism remains unchanged; the third possibility is progression to overt hypothyroidism.

In long term follow up study, women who initially had antithyroglobulin and antimicrosomal antibodies along with a serum TSH of greater than 6 μ U/ml developed overt hypothyroidism at the rate of 5% per year. No cases developed overt hypothyroidism in women with border line elevation of TSH (6 –10 μ U/ml) and only one women developed overt hypothyroidism who had antithyroid antibodies with normal TSH levels.³⁷

Other studies support progression to overt hypothyroidism at a rate of 7% per year in women with elevated serum TSH and high titers of antithyroid antibodies which ranges from 1 – 20% per year.^{38, 39} It is clear that the presence of antithyroid antibodies constitutes a significant risk factor for the development of clinically overt hypothyroidism.

Serum levels of triglycerides, total cholesterol and LDL cholesterol levels are elevated but are not as marked as in overt hypothyroidism. Some studies but not others have shown a decrease in LDL cholesterol and total cholesterol levels after treatment with levothyroxine.^{40,41,42}

G. Diagnosis

An elevated TSH level suggests thyroid failure and the FT₄ level determines the degree of failure.¹

Because of its great sensitivity and adequate specificity, the serum TSH level alone should be

measured in patients having hypothyroidism and in whom it needs to be excluded.⁴³ If TSH is normal, hypothyroidism is essentially ruled out and serum free T₄ (FT₄) rarely needs to be measured. Serum FT₄ level should be measured to differentiate overt hypothyroidism (subnormal FT₄) from subclinical hypothyroidism (normal FT₄). Subclinical hypothyroidism is usually indicated by a serum TSH level between 5mU/l –15mU/l, occasionally higher. The serum FT₄ level is by definition within normal range; it even tends to be below the mean of the euthyroid population. The serum TSH measurement may need to be repeated in patients with concurrent illness because it may be subnormal during illness and may remain transiently elevated during the recovery phase for a period of 4 weeks.

Measurement of thyroid antibodies (anti-thyroid peroxidase, antithyroglobulin) is neither sensitive nor specific. Only a minority of elderly patients with elevated antibody levels have hypothyroidism and only 40 – 70 percent of patients with hypothyroidism have elevated antibody levels. However, the measurement is prognostically significant because in patients with positive antibody titre, the rate of progression to overt hypothyroidism is much higher.

Serum cholesterol and creatine phosphokinase levels are elevated in hypothyroidism; these measurements are rarely useful diagnostically.⁴³

Hypothyroidism must be differentiated from sick euthyroid syndrome which is characterised by abnormal thyroid function tests seen in clinically euthyroid patients with severe non thyroid systemic illness.

Findings in sick euthyroid syndrome include a decrease in total and unbound serum T₄ levels with normal levels of serum T₄ and TSH and increased reverse serum T₃ (rT₃) but difficulty arises because of low serum T₃ and FT₃ levels in the most seriously ill patients. The serum TSH level may fluctuate from < 0.1 to > 20 mU/L. Diagnosis of hypothyroidism in critically ill patients can be made only if serum TSH level is markedly elevated (TSH > 20 mU/L) or if the free T₄ level is markedly subnormal (< 8 pmol/L); hypothyroidism is more likely when both findings occur together.

H. Screening

Screening asymptomatic elderly patients for primary hypothyroidism is controversial.

The American College of Physicians do not

recommend routine screening of asymptomatic patients because of presumed lack of demonstrated efficacy or proven benefit in the treatment of subclinical hypothyroidism. Based on the clear influence of age on the risk of development of hypothyroidism it is reasonable to screen all the elderly individuals for the possible presence of the disorder by measurement of serum TSH.³¹

The American Thyroid Association recommends screening all adults older than age 35 years for thyroid function every 5 years by measurement of TSH.¹¹

At this juncture evidence does not support routine universal screening for hypothyroidism but ongoing studies may provide support for screening in selected populations, especially elderly women and those at high risk of hypothyroidism eg. history of intake of amiodarone or lithium, history of thyroid surgery, radio iodine therapy or history of radiation to the head and neck.

I. Treatment of Hypothyroidism

Hypothyroidism is treated with levothyroxine preparations. It is important “to start low and go slow”. In the elderly, the dose requirement may also be lower because of increased half life i.e. approximately 9 days, by the 7th decade of life.⁴⁴

The usual starting dose is 25 µg daily and increment is done at an interval of 4 – 8 weeks until there is normalisation of TSH.

In the elderly, and for patients with ischaemic heart disease, initiating thyroid hormone replacement and increasing the dose needs to be cautious as angina and congestive cardiac failure may be exacerbated. A thyroxine starting dose as low as 25 µg on alternate days or 12.5 µg daily may be necessary when commencing treatment in this setting, with small dose increments every one or two months. Starting with low doses offers the opportunity to withdraw the medication more promptly if angina increases. Antianginal medications should be prescribed to patients with IHD for prevention of angina.

Hypothyroid patients with symptomatic ischaemic heart disease should be managed by an endocrinologist in collaboration with a cardiologist as these patients sometimes need coronary intervention such as coronary angiography and angioplasty or stenting and occasionally even coronary artery surgery, before the hypothyroidism can safely be treated.

Supportive care in the form of anti-bone resorption medicines such as calcium should be given concomitantly. Antianginal medications should be prescribed to patients with IHD for the prevention of angina that may be precipitated by levothyroxine.

In the elderly it may be important to consider other strategies to improve adherence to taking the medication such as prescribing in blisterpacks, or involving other members of the family or in supervision. Patients who forgot a dose can take it as a 'catch up' dose when they remember, even if it means taking two days' tablets at once.

It seems reasonable to treat patients who have TSH level that is consistently elevated above 10 μ U/ml specially if titers of antithyroid antibodies are increased. Also patients who complain of fatigue, dry skin, constipation, muscle cramps or other common symptoms of hypothyroidism may possibly benefit from treatment even if their TSH level is elevated only (5 –10 mU/L).

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