

Hypothyroidism

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Autoimmune thyroid disease (AITD), surgical or radioactive ablation of the gland, hereditary defects in hormone synthesis and drugs are causes that result in hypothyroidism.

The clinical and biochemical alteration resulting from deficient secretion of thyroid hormone is called hypothyroidism. The prevalence of hypothyroidism in literature is zero to four per 1000 in men and 3.3 to 20.5 per 1000 population¹. It is more common in women. The disease can occur at any age, but is described to occur commonly between 45 to 60 years in the western literature¹. Compared to this, our data of 404 hypothyroid Indian patients showed that 73 percent were between 20 to 50 years of age. The characteristic appearance of myxoedema is the result of long-standing primary hypothyroidism and is rare.

Primary Hypothyroidism

Primary (Thyroprivic): The disease called is “Primary” when direct involvement of thyroid causing destruction or damage causes hypothyroidism. Autoimmune thyroid disease (AITD), surgical or radioactive ablation of the gland, hereditary defects in hormone synthesis and drugs are causes that result in hypothyroidism, out of which AITD is the commonest. Goiter may be present during the early phase of autoimmunity, but the gland is usually atrophic at presentation.

Commonest cause of primary hypothyroidism in childhood to adulthood is AITD. Genetic predisposition to autoimmune disease is described. Activation of immune process takes place as in other autoimmune endocrine disorders. Both transient and permanent hypothyroidism can result. The different terminologies used to describe autoimmune hypothyroidism are Goitrous (Hashimoto's) thyroiditis, lymphocytic thyroiditis, Chronic fibrous thyroiditis and atropic autoimmune thyroiditis.

Autoimmune damage to functioning cells result in atrophy and hypothyroidism. Other factors that may have a role to play in autoimmunity are dietary iodide, drugs (amiodarone, contrast media), environmental pollution and stress. Association with other autoimmune disorders like IDDM, adrenal insufficiency, premature ovarian failure, rheumatoid arthritis and chronic active hepatitis are well described.

Postoperative hypothyroidism results from subtotal/total thyroidectomy for thyrotoxicosis or malignancy respectively. It is less frequent than post radioactive ablation and the incidence increases with duration of follow up. Almost all patients treated with radioactive iodine ablation develop hypothyroidism over a period of 10 to 15 years.

Postpartum thyroiditis and painless thyroiditis are variants of autoimmune thyroid disease. The immune reaction rapidly develops. Follicular cells are not destroyed, only damaged. An initial phase of thyrotoxicosis is followed by transient hypothyroidism lasting from two to eight weeks. Very often symptoms are too mild and the condition may go unrecognized. The hypothyroidism itself is because of the non-functioning of follicular cells damaged by the immune process. As soon as the cells recover, the function is regained and hypothyroidism remits.

Drugs: Amiodarone² and lithium³ are known to produce hypothyroidism in adults. Amiodarone has iodine in the molecular structure & this can either produce an iodine induced hypothyroidism or can precipitate autoimmune process in susceptible individuals. The condition is usually self limiting and recovery occurs after stopping the drug. Rarely there is permanent hypothyroidism. Lithium causes hypothyroidism by inhibiting the transport of iodide by the thyroid and may also induce chronic autoimmune thyroiditis.

Following the initial symptoms of weakness, fatigue, lassitude, weight gain and constipation, further symptoms develop. There is puffiness of face and intolerance to cold.

Clinical Features of Primary Hypothyroidism

Thyroid hormones are necessary for normal functioning of each and every cell in the body and hence in the initial stages, patients have vague symptoms of general weakness, increased fatigue and lassitude. Very often they are attributed to increasing age, excessive work or even stresses and strains of life. Generally, the physical appearance at presentation will depend on the duration and severity of disease.

Hypothyroidism can be goitrous as in Iodine induced and synthetic defects or agoitrous as in autoimmune involvement.

There is a gradual onset of symptoms due to gradually progressive thyroid damage. Following the initial symptoms of weakness, fatigue, lassitude, weight gain and constipation, further symptoms develop. There is puffiness of face and intolerance to cold. The skin is scaly, pale, cool to touch; hair is coarse, dry, brittle and hair loss over lateral aspect of eyebrow is considered a classical (though late) clinical feature. There is bradycardia and decreased exercise tolerance. The cold skin and pallor are due to poor peripheral circulation resulting from increased peripheral vascular resistance. Nearly 10 to 20 percent of patients are hypertensive³ at presentation. Long standing hypothyroidism may cause pericardial effusion^{5,6} rarely leading to cardiac tamponade.

Hoarseness of voice is another common complaint and is due to thickening of vocal cords resulting from deposition of hyaluronic acid as in the dermis. The tendon reflexes are delayed. Prolonged hypothyroidism can result in carpal tunnel syndrome and peripheral neuropathy. Rarely there is pseudohypertrophy of calf muscles and cerebellar ataxia.

Mental changes can sometimes be the presenting feature. There is slowness in speech and motor activities and there is decreased motivation. There is no interest in day to day activities and this is seen as laziness. Occasionally, severe depression or frank schizophrenia may lead to patient being seen in the psychiatric department. By this time other clinical features of hypothyroidism are usually present.

Females of reproductive age can present with irregular menstrual cycles (anovulatory) and infertility. Hence pregnancy is unlikely. If pregnancy does occur, there is increased risk of intrauterine fetal death, gestational hypertension and poor perinatal outcome⁷. Whether maternal hypothyroidism can result in fetal malformation and psycho-neurological changes is not clear. Rarely females can present with galactorrhoea due to long-standing hypothyroidism. This results from TRH induced stimulation of prolactin.

The clinical features are less classical in the elderly as compared to adults. Fatigue, weakness, cold intolerance, dry skin, constipation, mental deterioration and congestive cardiac failure gets attributed to aging or other pre-existing disorders⁸. Nearly 10 to 15 percent of elderly screened has been found to be hypothyroid and most have a positive antibody titer^{9,10}.

Very rarely, myxoedema coma may be the first presentation.

Subclinical Hypothyroidism

The combination of elevated serum thyrotropin and normal serum thyroxine is called compensated or subclinical hypothyroidism. Controversy exists regarding treatment of this condition. It is commonly seen in AITD. Females with TSH more than 10m U/L and/or positive thyroid microsomal antibodies and males regardless of antibody status are considered high risk for developing overt hypothyroidism¹⁰.

Secondary (Central) Hypothyroidism

Central hypothyroidism results due to pituitary disorders including tumor and Sheehan's Syndrome. This is generally associated with other hormonal deficiencies. Symptoms of tumor: like headache and visual disturbance may be the reason to seek medical advice.

It has also been noticed that as age advances, the dose requirement may come down. Hence regular monitoring is required. It is not advisable to withhold therapy in elderly for fear of side effects, as quality of life improves with correction of even mild hypothyroidism.

Clinical features are generally similar to those of primary hypothyroidism but are less pronounced. Major differences are: skin is pale and cool (but not coarse and dry). There is no change in voice; the blood pressure is low. The heart is small. There is no weight gain. Hypoglycemia can occur due to deficiency of both thyroid and adrenal hormones. Occasionally, hypopituitarism presenting with only thyroid axis involvement can present very similar primary disease.

Laboratory Investigation of Hypothyroidism

Primary

The only test required for confirming the diagnosis of overt primary hypothyroidism is TSH by IRMA/ICMA, when classical clinical features are present. This is associated with low FT4 and low FT3.

Laboratory investigations are dependent upon the stage of thyroid failure. The first suggestion of failing thyroid is shown by elevated TSH with normal total and free T4 and T3 (subclinical hypothyroidism). At this stage, the thyroid hormones are maintained by TSH drive. The hyperplasia of the still functioning cells maintains normal hormonal levels (hence called

Differential Diagnosis

It is not unusual for a hypothyroid patient to see a nephrologist first with suspected nephritic syndrome due to anasarca and vice versa. Normal TSH, TT4 and abnormal renal function tests including proteinuria, in nephritic syndrome can easily distinguish this.

Ruling out hypothyroidism sometimes may be required in severely ill patients. The FT4 may be on the lower normal range. TSH is high in primary hypothyroidism, but normal or low in illness. However, a pituitary disease is difficult to rule out and may require further investigations (Other pituitary axis evaluation and CT scan) if suspected.

In very young and very old, it is necessary to do thyroid function whenever suspected, as it is easily treatable disorder and clinical features may not always be classical.

Management

Thyroid hormone replacement should be instituted as soon as the diagnosis is established. The usual dose varies from 50 to 200 g/day. It is essential to treat with smallest dose that is required to have a normal TSH to avoid adverse effects of therapy on the bone and heart. Many (80 percent) of our patients required only 100 g/day. The TSH returns to normal 8 to 12 weeks and hence ideal time to monitor after initiation of therapy is three months. The commonest cause of poor response to treatment is noncompliance and this has to be kept in mind before increasing the dose of thyroxine. Proper education of patients and relatives regarding life long therapy is essential to ensure compliance.

It has also been noticed that as age advances, the dose requirement may come down. Hence regular monitoring is required. It is not advisable to withhold therapy in elderly for fear of side effects, as quality of life improves with correction of even mild hypothyroidism. Post surgical or radioactive ablation induced hypothyroidism requires higher dose as compared to Graves' treated with medical therapy.

In the elderly, the therapy should be started with very small doses of thyroxine and can be as low as 0.025 g/day, with very gradual increases of 0.025 g/day every 15 or 30 days. The TSH should be maintained, nearer the higher normal values. If there is associated cardiac disease, the starting dose should be extremely low (0.0125 g/day) with increases of 0.0125 g/day, once a month.

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