Epidemiology, Types, Causes, Clinical Presentation, Diagnosis, and Treatment of Hypothyroidism

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Abstract

Hypothyroidism is the condition when the thyroid gland is underactive. This reduces the thyroid gland's ability to function properly. It is a common endocrine condition characterized by hyposecretion of thyroid hormones, primarily thyroxine (T4) and triiodothyronine (T3). It affects people of all ages, but is more prevalent in women and the elderly. Hypothyroidism symptoms might go unreported, are nonspecific, and overlap with other illnesses, making it difficult to diagnose in some situations. Fatigue, weight gain, cold intolerance, irregular bowel movements, and dry skin are some of the most common symptoms. These disorders are generally caused by a poor metabolic rate in the bodyWeight gain results from a decrease in fat-burning rate and cold intolerance caused by the body's decreased heat output. Several causes can contribute to this syndrome, including autoimmune diseases, radiation therapy, thyroid gland removal operations, and certain drugs. Laboratory tests measuring thyroid hormone (T3 and T4) levels in the blood are used to diagnose hypothyroidism. Treatment usually entails lifelong hormone replacement therapy with synthetic thyroid hormone replacement medicine, such as levothyroxine, to help control hormone levels in the body. People with hypothyroidism may require medication dose adjustments over time. If hypothyroidism is not treated, it can lead to serious consequences such as mental retardation, delayed milestones, and heart failure in infants, as well as infertility, myxedema coma, and other difficulties in adults. The symptoms of hypothyroidism can be adequately managed with appropriate therapy, and the majority of persons with the illness can live normally. Lifestyle changes, such as eating healthier and exercising more frequently, can help manage symptoms and improve Life quality.

INTRODUCTION

Hyperthyroidism is a disorder in which the thyroid gland fails to produce enough thyroid hormones into the bloodstream. This slows metabolism. This is also known as thyroid hypoactivity. Hypothyroidism can cause fatigue, weight gain, and an inability to handle cold weather. Hypothyroidism is an endocrine condition in which the thyroid gland fails to produce an adequate supply of thyroid hormones.[1]

Primary hypothyroidism is most commonly caused by iodine deficiency in iodine-deficient geographic locations around the world. Autoimmune thyroid disorders are the major cause of hypothyroidism in iodine-sufficient areas. Hashimoto thyroiditis is the most frequent cause in the United States, and it has a strong link to lymphoma. Iodine fortification and the advent of new iodine-deficient areas can both have an impact on hypothyroidism etiology locally.

A frequent endocrine condition called hypothyroidism is brought on by a drop in thyroid hormone levels, which lowers basal metabolism and effective energy usage. Thyroid hormone decreases can be caused by the thyroid gland producing less (primary), the pituitary gland producing less thyroid- stimulating hormone (TSH) (secondary), or the hypothalamus producing less thyrotropin-releasing hormone (tertiary). Subclinical hypothyroidism and myxedema are two extremes of hypothyroidism severity. Weight gain, hair loss, sadness, constipation, cold intolerance, and nonpitting edema are only a few of the clinical signs and symptoms of hypothyroidism, which has wide-ranging systemic consequences that affect most organ systems.[2,3]

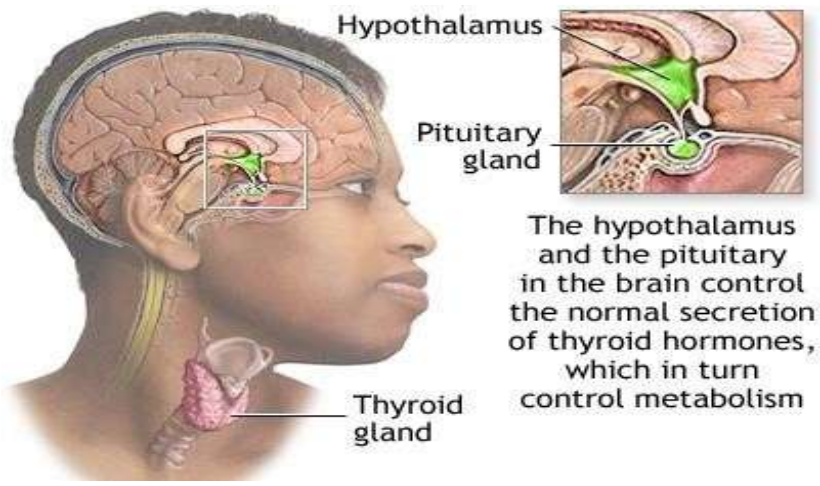

FIG 1

Patients with hypothyroidism are typically treated with levothyroxine, which replaces thyroid hormone. However, a significant percentage of levothyroxine-treated patients continue to experience problems even after meeting the biochemical therapy goals. This has raised concerns

about whether levothyroxine treatment is adequate for all patients or if other treatments (such as combining it with liothyronine preparations) could be used instead. Pregnant women and children with hypothyroidism are treated as distinct subjects and have been covered elsewhere.[4]

Type of Hyperthyroidism

There are three type of Hyperthyroidism : primary , secondary and tertiary Hyperthyroidism.

Primary Hyperthyroidism: The thyroid's own distraction prevents the thyroid gland from producing enough thyroid hormone in primary hypothyroidism. Iodine and radioiodine deficiencies, as well as autoimmunity, are the usual causes of this distraction. This indicates that the issue stems from the thyroid itself.It is still uncertain what precise mechanisms cause Hashimoto's thyroiditis, however both genetic and environmental variables play a role. In order for us to better understand the disease and attempt to avoid it, additional research into its mechanisms is required. The genome- wide association studies identified five genetic variations for thyroid peroxidase antibodies, which were used to create an enhanced genetic risk score. This score has demonstrated a graded link between elevated TSH levels and clinical hypothyroidism [5’6]. Thyroid peroxidase antibody levels are lower in smokers than in non-smokers, and the incidence of autoimmune thyroiditis rises after quitting smoking [7]. Because lithium affects thyroid hormone synthesis and release, it also plays a role in hypothyroidism .Six percent of individuals in a large population-based cohort study needed levothyroxine medication within 18 months of starting lithium therapy.

Hypothyroidism often occurs with radioiodine therapy, a hemithyroidectomy, cancer surgery, or neck radiation therapy [8]. Many teason causes the hypothyroidism disease in the human and produce the symptoms of this disease Approximately 75 percent of people with Grave's disease will eventually develop hypothyroidism, even with low doses of radioiodine. Reportedly, 7% of patients with isolated toxic nodules and 50% of individuals with toxic nodular goiter who get treatment also experience hypothyroidism. A meta-analysis research found that 20% of patients had hypothyroidism following hemithyroidectomy. Other major causes of hypothyroidism include infiltrative disease and transient thyroiditis.

Secondary hypothyroidism : Thyroid stimulating hormones (TSH) are not secreted by the pituitary gland in secondary hypothyroidism. The thyroid is not sufficiently stimulated by the pituitary gland to create hormones. Usually, a pituitary tumor is the source of this. In other words, the pituitary gland is the cause of the issue rather than the thyroid. Although

it is rare, central hypothyroidism affects both sexes equally. Pituitary and hypothalamic disorders are more commonly associated with it, though it typically encompasses both. The biochemical features of central hypothyroidism include extremely low levels of free T4 and low levels of TSH. TSH levels are occasionally somewhat higher, most likely as a result of reduced bioactivity. More than half of cases of central hypothyroidism are caused by pituitary adenomas. Other causes of central hypothyroidism include damaged pituitary gland and hypothalamic functions due to pituitary apoplexy, head trauma, Sheehan's syndrome, radiation, various surgical operations, heredity, and infiltrative illness.[9,10,11]

Tertiary Hyperthyroidisms : When tertiary hypothyroidism occurs, the pituitary does not deliver enough TSH to stimulate the production of thyroid hormones (T3 and T4) because the hypothalamus does not release enough thyrotropin-releasing hormone. While tertiary hypothyroidism is uncommon, when it does happen, it is frequently brought on by a mass or tumor on or close to the hypothalamus.[12]

Causes of Hyperthyroidisms

According to its aetiology, hypothyroidism can be classified as primary, secondary, tertiary, or peripheral

Primary hypothyroidism is the most prevalent type, and it accounts for about 99% of cases. Of these, 95% are caused by Hashimoto's disease, a chronic autoimmune illness that destroys thyroid follicular cells [13]. Dietary iodine shortage, which occurs after ablative treatment for hyperthyroidism (i.e., total thyroidectomy), or an adverse pharmacological reaction (e.g. to amiodarone used to treat arrhythmias or lithium used to treat bipolar disorder) are additional reasons of primary hypothyroidism. TSH can be further classified as "overt" when it is elevated and free levels are low, or "subclinical" when it is elevated but free within the normal reference range.[14]

Although primary hypothyroidism affects both men and women equally, secondary and tertiary hypothyroidism, also known as central hypothyroidism, develop after decreased thyroid stimulation due to dysfunction outside the thyroid, either in the anterior pituitary gland or the hypothalamus, respectively [6,8]. The most common cause of central hypothyroidism is pituitary dysfunction, with 50% of cases being due to pituitary adenoma. However, hypothalamic tumors, certain infiltrative disorders (like amyloidosis), physical trauma, surgery, or even medications (like cocaine, glucocorticosteroids, and metformin) can also cause this condition [15,16]. In any case, reduced production of TSH and/or TRH eventually results in hypothyroidism and decreased thyroid hormone synthesis and release.

Lastly, when free-circulating levels of T3, T4, and frequently TSH are adequate, peripheral hypothyroidism develops. Even when a patient's biochemical findings are normal, hypothyroidism symptoms can still arise because of either thyroid hormone deactivation due to increased production of "deiodinase 3" by some tumor cells or thyroid hormone resistance caused by genetic abnormalities in peripheral tissues. These symptoms differ from person to person and are probably influenced.[17]
[18]Furthermore, there is no known direct cause for congenital hypothyroidism, which affects about 1 in 2,000–3,000 babies born in the UK. This condition occurs when the thyroid gland is missing, undeveloped, or unable to synthesize thyroid hormones.

Signs and symptoms :- Due to the subtle nature of the disease's beginnings, hypothyroidism's non- specific symptoms are sometimes overlooked during patient evaluations or mistakenly attributed to aging. The table summarizes the common signs and symptoms of hypothyroidism.[18,19].

General	Weary Hoarse voice
Cardiac	Bradycardia Diastolic elevated blood pressure Effusion in the pericardium

gastrointestinal	Gainingweight Reduceappetite Being constipated Distension in the abdomen
Neuromuscular	Depressed mood increased cold sensitivity Join the misery. Neuropathy that is peripheral paraesthesia
Reproductive	Infertility erratic menstrual cycles
Skin appearance	Goitre less perspiration Coarse hair A yellow complexion

Similar symptoms to those of primary hypothyroidism are likely to be present in patients with central hypothyroidism. They may, however, also have other symptoms, such as diplopia (double vision), general symptoms (such as frequent headaches), and other visual abnormalities [20.21]. Specific signs of pituitary malfunction include acromegaly, amenorrhea, Cushing's disease, and erectile dysfunction .There aren't many telltale signs of congenital hypothyroidism. While some newborns have difficulty sleeping and feeding, this is not unusual. For this reason, around five days of age, all neonates have a heel-prick test to screen for a variety of disorders, including hypothyroidism.

Diagnosis :- The thyroid should not be overlooked during clinical examinations and consultations since symptoms of hypothyroidism are comparable to those of aging and menopause, as well as diseases including anemia, diabetes mellitus, Addison's disease, vitamin deficiencies, stress, and depression
Biochemical tests of TSH and free T4 levels (FT4), in addition to the patient's presenting symptoms, are used to diagnose hypothyroidism [23]. As opposed to inert protein-bound hormone, testing for the "free" hormone ideally yields a more accurate diagnostic result because it only indicates hormone that is ready for action.[24].

According to guidelines from the National Institute for Health and Care Excellence (NICE), biochemical testing for thyroid dysfunction should be made available to all patients who present with new-onset atrial fibrillation, type 1 diabetes, or other autoimmune disorders. Patients who have unexplained anxiety and depression should also be evaluated for thyroid dysfunction [25].

If the TSH level is within the reference range of 0.4–4 mU/L, the initial test is adequate to rule out primary hypothyroidism. To validate the primary aetiology, a free T4 level is measured if TSH is elevated, preferably from the same sample. The thyroid gland's incapacity to react to this sufficient stimulation and the proper hypothalamic-pituitary response to low hormone levels would be indicated by a high TSH and a low FT4. However, in order to rule out possible hyperthyroidism and look for secondary hypothyroidism, a free T3 and FT4 level should be requested if TSH is low, preferably from the same sample [26,27]. FT3 is not thought to be diagnostically significant for hypothyroidism because it is consistently within range, even in cases of severe hypothyroidism [28]. For FT4, the reference ranges are 9–25 mol/L, and for FT3, they are 3.5–7.8 pmol/L. For patients who develop new symptoms or whose symptoms worsen,

these tests should be re-checked no sooner than six weeks following initial testing, as re-testing any sooner is unlikely to show clinically significant changes. Although NICE guidance suggests a TSH level should only be taken initially for people not thought to be suffering from central hypothyroidism, this can sometimes lead

to a delayed diagnosis, especially in primary care[29].Therefore, in clinical practice, many centres will test TSH and FT4 at presentation of symptoms as standard assessment.

The aim of treatment is to effectively replace thyroid hormones through pharmacological intervention, to resolve symptoms and bring TSH levels back within standard range.

First-line treatment for primary and central hypothyroidism in all adults and children is oral levothyroxine, a synthetic form of T4, which provides replacement hormone to correct the deficiency in production[13]. Starting dose in people aged under 65 years with no pre-existing cardiovascular disease (CVD) is 1.6 micrograms/kg daily, rounded to the nearest 25 micrograms [30]. However, as overtreatment with levothyroxine can increase cardiac workload, people aged over 65 years or with pre-existing CVD should start at 25-50 micrograms daily, which can then be titrated up slowly every 4 weeks in steps of 25 micrograms until therapeutic effect is achieved For congenital hypothyroidism, starting doses of levothyroxine are given at 10–15 micrograms/kg per day for the first 3 months of life, after which the dose is adjusted dependent on TSH and free T4 levels.

Levothyroxine is contraindicated in individuals with hyperthyroidism, those who have experienced hypersensitivity reactions and in patients with uncontrolled adrenal insufficiencyPatients with adrenal insufficiency should be started and stabilised on corticosteroid therapy prior to commencing levothyroxine to reduce the precipitating adrenal crisis on levothyroxine initiation

For those truly intolerant of levothyroxine, liothyronine is a synthetic form of T3 that displays a similar pharmacological action. Liothyronine is five times more potent, with a more rapid onset of action metabolism. While there has previously been debate regarding the use of liothyronine as monotherapy for management of hypothyroidism, or even combination treatment with levothyroxine, the Royal College of Physicians strictly advises against this, owing to a lack of clinical evidence[30,31]. Although there is a small cohort of patients who require liothyronine, because of this lack of clinical evidence and greater cost, specialist endocrinologist assessment and consultation is vital for use within hypothyroidism management.

Pharmacists experienced with thyroid disorders may provide direct patient care through provision of thyroid clinics in primary or secondary care, assessing and managing patients as part of their multidisciplinary teams.[31,32]

Medications counselling

When it comes to repeat supplies, community pharmacists are probably the only healthcare professional (HCP) that patients meet in person and are frequently the last HCP a patient sees before starting new therapies. In order to encourage patients' adherence during treatment, they are consequently in a prime position to offer counseling regarding possible side effects [31] Lifelong levothyroxine therapy is frequently needed to treat hypothyroidism, which can make it difficult for patients to stick to their treatment plans. Even patients who receive the right counseling may not be able to take their prescription as prescribed

Levothyroxine has been demonstrated to be safe and effective when administered in these situations in once-weekly dosages with the help of a family member or community team . Talking about drug interactions is essential while providing pharmaceutical counseling. Cholestyramine, calcium supplements, and ferrous sulphate can all decrease levothyroxine absorption [15,27]. Hepatically, levothyroxine is converted to active T3 as a prohormone. Thus, medications that alter liver enzymes, such rifampicin, carbamazepine, and phenytoin, may also change therapeutic levels . Levothyroxine absorption might be decreased by up to 80% when food is consumed . Patients have historically been advised to take levothyroxine as soon as they wake up, half an hour before breakfast. Nonetheless, research has indicated that levothyroxine taken in the evening or right before bed offers comparable biochemical adjustments to thyroid function tests [28]. It is recommended that patients take this drug every day, on an empty stomach, at a time that

works best for them .

Complications

Pregnancy :- Low levels of T4 can decrease fertility, damage the fetus throughout pregnancy, and in certain situations, result in miscarriage [30,31]. If a patient has thyroid disease or has had thyroid disease in the past and is considering a pregnancy, they should speak with their doctor and have their TSH levels checked often . When patients learn they are pregnant, the British Thyroid Foundation advises them to immediately raise their levothyroxine dosage by 25–50 micrograms and schedule a TSH test [30]. With the goal of reaching a TSH level of less than 2.5 mU/L in the first trimester and less than 3.0 mU/L in the second and third trimesters, TSH levels should be checked every 4-6 weeks during pregnancy [32].

Most individuals are able to resume their prior optimal dosage of TSH, but a follow-up assessment is necessary a few weeks after delivery. It is important to encourage patients who want to breastfeed and to let them know that taking levothyroxine while nursing is safe.

Myxoedema coma :- Approximately 40% of patients with severe hypothyroidism are not aware of their thyroid failure before being admitted, and myxoedema coma is an uncommon consequence that affects 0.22 people per million year in the Western world . With high mortality rates of 25– 60%, this severe form of hypothyroidism is frequently deadly and is characterized by diminished consciousness, hypothermia, macroglossia, periorbital oedema, and coarse hair. Intravenous levothyroxine and, in more extreme situations, liothyronine are part of the first treatment Because levothyroxine medication might worsen an Addisonian crisis, intravenous hydrocortisone is also administered until adrenal insufficiency is ruled out. As hypothyroidism is under control, patients can be maintained using oral levothyroxine[33.34]

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