



Review Article

Hypothyroidism: If not treated in time, it leads to an underperforming population

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ABSTRACT

Thyroid dysfunction has detrimental effects on human health especially in pregnant women, children, patients with cardiovascular and other diseases. Hypothyroidism (HT) is the most common thyroid disease (TD) that occurs due to low circulating thyroxine and affects human mental and physical health. The diagnosis of hypothyroidism (HT) is based primarily on biochemical parameters, with thyroid-stimulating hormone (TSH) levels (elevated above normal) being the most sensitive indicator of thyroid status. It can present with a number of symptoms, such as poor ability to tolerate colds, a feeling of tiredness, constipation, slow heart rate, depression, weight gain, and low cognitive function. Its clinical manifestations in the elderly may be less obvious than other conditions related to aging. Thyroid function test interpretation may be altered due to the presence of non-thyroidal illness. Special considerations may apply in planning treatment due to changes in the metabolic clearance of thyroid hormone, drug interactions, and potential adverse reactions. In this article we will discuss the burden and impact of diseases in society, also discussing how low hormones affect different organs and the physiology of the body. We also discussed how to harm the HT in our generation.

Keywords: Hypothyroidism, cognitive function, mental health, physical health.



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Introduction

Epidemiological Aspect: Thyroid disorders affect a large proportion of the population and are the most common endocrine disease worldwide. The incidence of HT is rapidly increasing due to the availability of facilities for the detection of disease and increased life expectancy of the population globally, this has been described by authors like Jeffrey R et al (1). Worldwide more than one billion people are estimated to be iodine-deficient, however, it is unknown what the exact percentage of hypothyroidism. In the United States, one study reported HT occurs in 0.3–0.4% of people (2). Subclinical hypothyroidism, a milder form of hypothyroidism is marked by normal thyroxine levels and an elevated TSH level was found in 4.3%–8.5% of people in the USA (2). Hypothyroidism (both overt and subclinical) is more common in women than in men. People over the age of 60 are more commonly affected (3). Increased iodine intake appears to cause an increase in the prevalence of hypothyroidism (4). The American Thyroid Association reported that 20 million Americans have some form of thyroid disease and that more than 12% of US residents will develop thyroid disease at some point in their lives (5).

A meta-analysis of the epidemiology of thyroid dysfunction in European was conducted in 2014. The authors (6) stated that the prevalence of undiagnosed thyroid dysfunction was analyzed in 7 studies, with an average score of 6.71%, in which 4.94% and 1.72% were found to be undiagnosed hypothyroidism and hyperthyroidism, respectively. The prevalence of previously diagnosed and undiagnosed thyroid dysfunction was assessed in 9 studies, with an average score of 3.82% (6). Another study in India done by Sangeeta Pahwa, and Sabia Mangat found that the Prevalence of thyroid dysfunction was high in the pregnant study group in first-trimester pregnant women, with subclinical hypothyroidism in 6%, overt hypothyroidism in 2% (7).

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Meta-analysis was done recently in Europe (2019), which included 20 studies, showing a 4.7% prevalence of undiagnosed total (subclinical plus clinical) hypothyroidism in Europe. Among them 0.65% present undiagnosed clinical hypothyroidism and 4.11% present undiagnosed subclinical hypothyroidism (8).

A study done by Mendes D. reported (9) several factors such as age, gender, ethnicity, and geographical location may affect the prevalence of thyroid dysfunction. The geographical location appears to be associated with dietary iodine intake. They also find the prevalence of hypothyroidism is usually higher in women than in men among individuals ≥ 65 years of age.

In Bangladesh actually, we have no population-based study, but our clinical experience says a higher rate of clinical and sub-clinical hypothyroidism in our population with the maximum number of patients remaining undetected. According to a study done (10) by Das CK and his group show in Dhaka City, hypothyroid was found in 3.8%, and subclinical hypothyroid was found in 3.46 %, 16% of Bangladeshi pregnant women are suffering from thyroid disorders, 7.3% hypothyroidism and 3% hyperthyroidism. About 20% of the population suffers from TD in their lifetime.

Main causes of Hypothyroidism: Autoimmune thyroiditis is the number one cause of HT among the elderly, as it is in younger persons. Primary HT is a prevalent disease globally. It may be endemic in iodine-deficient areas. It is also a common disease in iodine-sufficient regions as reported in a population-based study by Wiersinga WM (11).

Carle A et al., (12) noted in 2016 that about 57% of patients presenting with primary hypothyroidism carried a diagnosis of autoimmune thyroiditis, while 32% carried a diagnosis of postsurgical HT and 12% had a diagnosis of post-radioiodine hypothyroidism. Only 2% of the patients in this referral population presented with documented evidence of secondary hypothyroidism. The incidence of post-ablative HT has also been noted in good numbers in society.

Other important reasons for HT are congenital defects in thyroid hormone biosynthesis, iodine deficiency, and iodine excess. Drugs: antithyroid agents, lithium, natural and synthetic goitrogenic chemicals, and tyrosine kinase inhibitors are also reported as causes of Hypothyroidism.

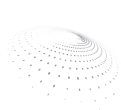
Pathophysiology of Hypothyroidism on different organs and functions

Thyroxine is a master hormone working on every cell, system, and organ from foot to head. The deficiency of thyroid hormone causes negative effects on almost every cell, system and ultimately there is a mild to severe detrimental effect on body physiology leading to physical and mental disability. Here we will discuss some of the pathophysiology of HT.

Skin: The characteristic pathologic finding in hypothyroidism is a peculiar mucinous nonpitting edema (myxedema), which deposits in the dermis like many other many organs. Myxedema is due to the accumulation of hyaluronic acid and other glycosaminoglycans in the interstitial tissue. Hydrophilic molecules hold water. There is hyperkeratotic plugging of sweat glands and hair follicles. The dermis is edematous, and the collagen fibers are separated, swollen, and frayed (13). Skeletal muscle cells are also swollen and appear grossly to be pale and edematous.

Voice: The voice is husky, low-pitched, and coarse. The speech is deliberate and slow. Often there is difficulty in speaking. Certain words are stumbled and slurred, as in alcoholic intoxication. The enlargement of the tongue and thickening of lips may be caused behind.

Renal: The kidney is grossly normal in HT. The blood vessels often show prominent atherosclerosis in HT. Salomon MI, DiScala V, Grisham E, et al; studied a long time ago stated that light and electron microscopic study of renal biopsy samples have shown thickening of the glomerular and tubular basement membranes, a proliferation of the endothelial and mesangial cells, intracellular inclusions, and extracellular deposition of



amorphous material with characteristics of acid mucopolysaccharides in HT (14). Clinical evidence of renal failure is not often found, but laboratory examination may disclose certain changes from normal renal functions serum creatinine is raised by 10-20%, normalizing after L-T4 treatment.

Metabolic side hypothyroidism: Energy. Thyroid hormone deficiency slows energy metabolism as a result there was a decrease in resting energy expenditure, oxygen consumption, and utilization of substrates. There was also reduced protein metabolism (15).

Carbohydrate. In HT glucose absorption from the intestine is slower than in normal conditions. Glycosylated hemoglobin is normal (16). The occurrence of hypoglycemia in hypothyroid patients should alert the physician to concomitant diseases (e.g., hypopituitarism). The development of hypothyroidism in patients with insulin-dependent diabetes mellitus may require lowering the insulin dose to counteract the decreased rate of insulin degradation.

Lipid. Biosynthesis of fatty acids and lipolysis are reduced. The lipid changes bear in general a reciprocal relationship to the level of thyroid activity. The increased serum cholesterol in hypothyroidism may represent an alteration in a substrate steady-state level caused by a transient proportionally greater retardation in degradation than in synthesis (17).

Neurologic aspect: A tendency to poor coordination was noted originally by the Myxoedema Commission (18) and described by the study of a series of myxedematous patients with ataxia, intention tremor, nystagmus, and dysdiadochokinesia. Ataxia has been noted in 8 percent of a large series of hypothyroid patients. These symptoms show a prompt and definite decrease after replacement therapy with thyroid hormone (19).

Sensory events: Numbness, tingling, and painful paresthesias are frequent and are especially common in HT after surgery or after radio-iodine therapy. Paresthesias were present in 79% of patients (19). A metachromatic infiltration has been found in the lateral femoral, cutaneous nerve, and sural nerve, there together with axon cylinder degeneration (20).

Mental Symptoms. Murray IPC reported in his study in 1961 (20) that the mental condition of patients with overt hypothyroidism may be one of early presentation. Memory is usually impaired and attention think was reduced. The emotional level usually seems low. The cognitive function of patients with moderate to severe hypothyroidism was low performing, with recent memory loss, reduced attention span, and slow reaction time (21).

Psychiatric: Hypothyroidism may present with the psychiatric symptom of depression or dementia (22) Patients are generally akinetic, though isolated case reports appear of patients who became hypomanic and agitated. It has been reported that psychosis with hallucinations may occur (23). Every patient with depression is to be evaluated for HT (24). Cerebral blood flow, oxygen consumption, and glucose consumption have been reported to be diminished in proportion to the drop in metabolism in the rest of the body.

Cardiovascular manifestations: Danzi S, Klein I, Kilein I, Danzi S (25) stated hypothyroidism decreases tissue thermogenesis by 5-8% and increases resistance in peripheral arterioles through the direct effect of T3 on vascular smooth muscle cells. Usually, diastolic blood pressure rises and the afterload of the heart increases. Cardiac chronotropy and inotropy are reduced.

Systemic cardiovascular changes: Pulse rate and stroke volume are diminished in HT and cardiac output is accordingly decreased. The contractility of the myocardium is low. There is also a steep decline in the circulatory load so that the circulation rarely fails until very late in the disease. Myocardial adenyl cyclase levels are reduced (26).

Cardiomegaly. In HT it embraced dilatation of the left and right sides of the heart, slow, indolent heart action with normal blood pressure, and lowering of the P and T waves of the electrocardiogram. After treatment with thyroid hormone there was a return of the dilated heart to somewhere near normal size, a more rapid pulse without

changes in blood pressure, and a gradual return of the P and T waves to normal. These findings have been confirmed and extended (27). Pericardial effusion was reported to occur in HT and explained the increase in the transverse diameter of the heart shadow in R-ray. Effusion frequently plays a role in the increase in the size of the heart shadow (28).

Angina pectoris. In a few cases, angina pectoris is encountered in myxedema. There is angina or angina-like pain present before treatment (29). This generally indicates the presence of significant coronary artery disease since there is inadequate myocardial oxygenation despite reduced cardiac output and O₂ utilization (30).

Muscles. Muscle symptoms like myalgia, muscle weakness, stiffness, cramps, and easy fatiguability are prevalent in HT patients. Weakness in one or more muscle groups is present in 38% as evident from manual muscle strength testing. The symptoms are aggravated by exposure to cold (31).

GI system: Anorexia and constipation is seen in almost every case of HT. Anorexia is interpreted as the reflection of a reduced food requirement resulting in constipation. Constipation also results from a lowered food intake and decreased peristaltic activity. Even two-thirds of patients have reported weight gain, which is of moderate degree and due to the accumulation of fluid rather than fat. Dysphagia or heartburn may be due to disordered esophagus motility.

HT patients tend to drink small amounts of water and have diminished urinary output (32). Clinical evidence of renal failure is not often found, but laboratory examination may disclose certain departures from normal renal function; serum creatinine is raised by 10-20%, normalizing after L-T₄ treatment. Serum cystatin C is strongly influenced by thyroid function, and it may give erroneous results for assessing renal function in hypothyroid patients (33).

Male reproductive system: The effect of HT on human spermatogenesis is evident, sperm morphology was significantly affected by HT. Primary hypothyroidism results in a decrease in sex hormone binding globulin (SHBG) and thereby in total testosterone concentrations in serum; free testosterone is either normal or reduced in approximately 60% of hypothyroid males (34, 35).

Female gonads and reproduction: In hypothyroid women sex hormone binding globulin is reduced and so are serum estradiol, estrone, and testosterone (36). A recent study shows that serum TSH levels are a significant predictor of fertilization failure in women undergoing in vitro fertilization (IVF). There is a known association between hypothyroidism and decreased fertility. A particular study reports that 34% of HT women became pregnant without treatment: 11% of them had overt and 89% had subclinical hypothyroidism (37). So, hypothyroidism does not always cause infertility.

Pregnancy: If HT is not treated in time adverse outcomes for mother and child are evident from many studies. A review of studies on the diagnosis and treatment of thyroid diseases during pregnancy and postpartum have been published in updated guidelines (38). The study shows if hypothyroid women become pregnant and maintain the pregnancy there is an increased risk for early and late obstetrical complications. There is an increased incidence and prevalence of miscarriage, anemia, gestational hypertension, placental abruption, and postpartum hemorrhages. These complications were more common with overt than with subclinical HT. This study also reported that adequate thyroxine treatment reduces risk of a poorer obstetrical outcome. Untreated maternal overt hypothyroidism is also complicated with bad neonatal outcomes such as premature birth, low birth weight, and respiratory distress.

Hypothyroid mothers' children are at risk of physical and mental problems. A number of studies were done in different institutes. The study done by Man et al., (39), Rovet et al., (40), and Pop et al., (41) methodically studied that children born to HT mothers had a significantly increased risk of low IQ scores, neuropsychological developmental indices and learning abilities. They also showed that the IQ scores of untreated women with

hypothyroidism were seven points below the mean IQs of children of healthy women and women treated with thyroxine. This risk also belongs to children born not only to untreated women but also women with suboptimal treatment. So, for future healthy generations, adequate measures are required to detect hypothyroidism in expecting mothers.

Respiratory: Wilson and Bedell (42) in their study found a normal vital capacity of lung and arterial PCO₂ in 16 patients. They also found a decreased maximal breathing capacity, decreased diffusion capacity, and decreased ventilatory response to carbon dioxide. The decreased ventilatory drive is present in about 33% of hypothyroid patients, and the response to hypoxia returns rapidly by a week of thyroxin treatment. Weakness of the respiratory muscles may be a cause of alveolar hypoventilation. Radiologic lung disorders suggestive of fibrotic disease are with severe HT. It usually resolves with levothyroxine therapy (43). Myxedematous patients are more subject to respiratory tract infections.

Diabetes: In HT Reduced glucose absorption from the gastrointestinal tract accompanied by prolonged peripheral glucose accumulation, gluconeogenesis, diminished hepatic glucose output, and reduced disposal of glucose are hallmarks of hypothyroidism (44). In overt or subclinical hypothyroidism insulin resistance leads to glucose-stimulated insulin secretion.

Screening for Hypothyroidism: Helfand M and Capro LM did a screening of the adult population in 1990 and reported the sensitive TSH assay may be used for screening if required in the adult population. Case-finding strategies have been carried out successfully. By screening unknown hypothyroidism was found in 0.64% of screening for cervical ca, 0.45% of women attending a primary health care unit, and subclinical hypothyroidism in 1.6%. Patients admitted to geriatric units also benefit from routine testing as 2% to 5% have treatable thyroid disease, but patients hospitalized with acute illness do not benefit from routine thyroid function tests due to frequent interference of test results by the sick euthyroid syndrome (45, 46).

Conclusions: The thyroid hormone is a metabolic hormone that works in every area of the body. It is essential for neurodevelopment and neuronal function. It is working on cells for their energy and metabolism, so any deprivation of thyroid hormone can lead to harmful effects on the body. So, hypothyroidism can lead to low performance, low IQ, and a depressed population.

Declaration

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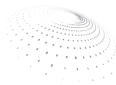
Ethical Statement: Not required.

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